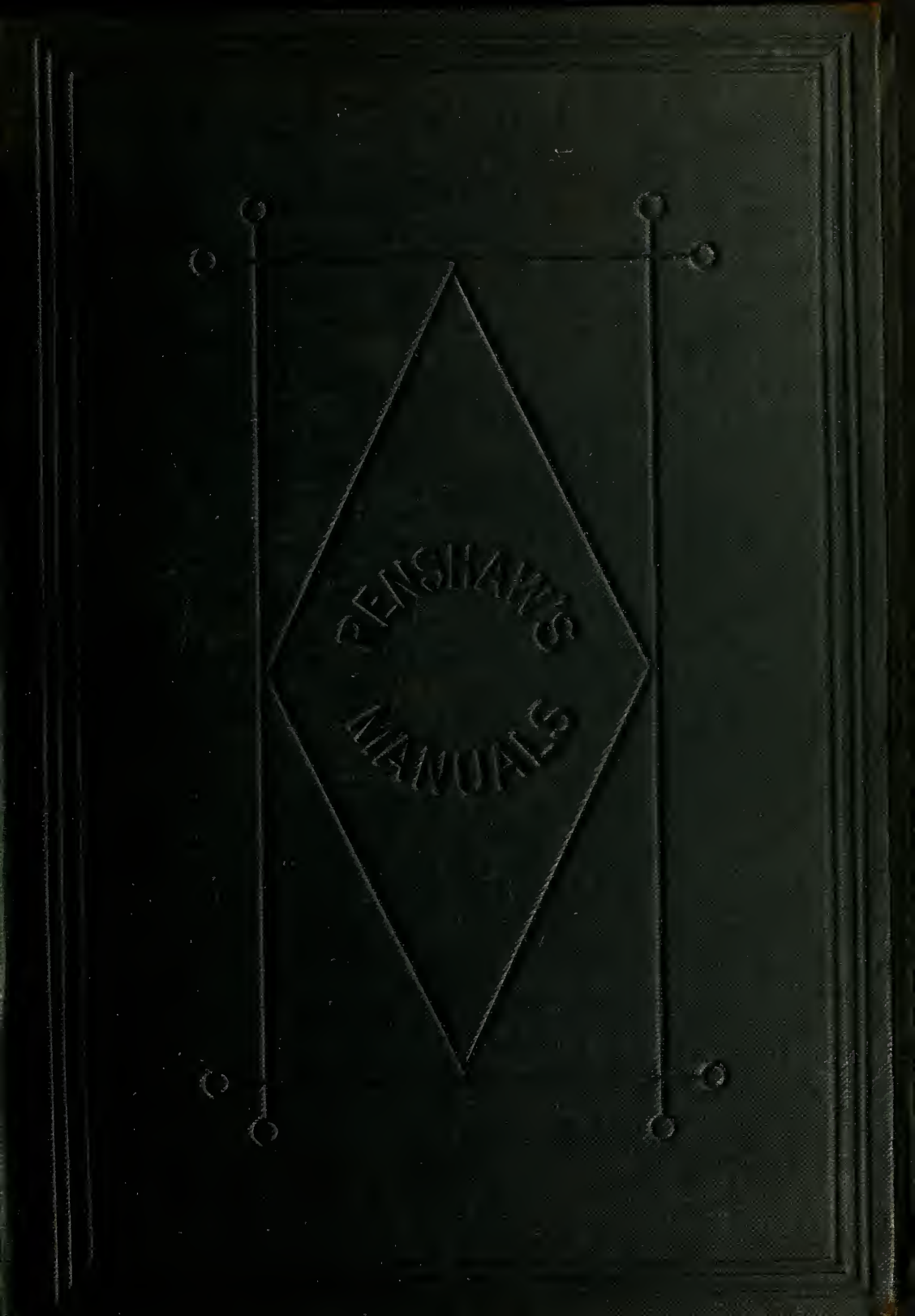

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AN INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.



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EXPLANATION OF PLATE.

FIG. 1.—STAPHYLOCOCCUS PYOGENES AUREUS. Culture in nutrient agar-agar. It will be noted that the orange colour is limited to the surface, the deeper portions of the growth occurring along the line of puncture being white (see p. 348).

FIG. 2.—BACILLUS ANTHRACIS. Culture in nutrient agar-agar. The growth covers the surface, and extends along the line of puncture in the form of a thick white streak, with finer streaks spreading at right angles from it, especially in the upper part (see p. 357).

FIG. 3.—THE BACILLUS OF MALIGNANT ŒDEMA. Culture in nutrient agar-agar. The growth occurs in that part of the line of puncture which is furthest from the air. Here it has a somewhat irregular outline and jagged edge. When traced upwards, it soon diminishes to a just perceptible tract. There is a characteristic development of air-bubbles in the neighbourhood of the growth (see p. 370).

FIG. 4.—BACILLUS DIPHTHERIÆ. Culture on Lœffler's blood-serum. This drawing is made from two separate cultures. The outlying grey spots, with the centre rather more opaque than the periphery (p. 365), is the form generally seen in primary cultures. The continuous line of growth represents a common form assumed in secondary and subsequent cultures (see p. 363).

FIG. 5.—THE SPIRILLUM OF CHOLERA. Culture in nutrient gelatine, at end of second day. Liquefaction has occurred at the upper end of the puncture, and a bell-shaped cavity is produced. The principal part of the culture lies in the lower part of this depression and in the upper part of its corkscrew like termination (see p. 370).

FIG. 6.—BACILLUS TUBERCULOSIS. Culture on glycerine-agar. The greater part of the growth consists of opaque, greyish or yellowish, heaped-up masses; but at the periphery, thin flakes or scales, which are very characteristic, can be seen (see p. 395).

AN INTRODUCTION

TO

PATHOLOGY AND MORBID ANATOMY.

BY

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PHYSICIAN AND SPECIAL LECTURER ON CLINICAL MEDICINE AT CHARING CROSS HOSPITAL, AND PHYSICIAN TO THE HOSPITAL FOR CONSUMPTION AND DISEASES OF THE CHEST, BROMPTON.

EIGHTH EDITION,

REVISED AND ENLARGED BY

H. MONTAGUE MURRAY, M.D., F.R.C.P.

PHYSICIAN TO OUT-PATIENTS, AND LECTURER ON PATHOLOGY AND MORBID ANATOMY AT CHARING CROSS HOSPITAL.

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PREFACE.

The last edition of this text-book was so thoroughly revised by Mr. Stanley Boyd that my task in editing the present issue has been comparatively light. The rapid accumulation of facts, and the consequent changes in opinion which have distinguished many departments of pathology, have, however, rendered it necessary that several new sections should be added, and several old ones rewritten or withdrawn. In making such changes as seemed advisable—and they occur on every page—I have adopted Dr. Green's concise and lucid sentences as my model, so that no disadvantages should accrue from the admixture of different styles of composition.

In view of the existence of many larger and more elaborate treatises on pathology, it has seemed unnecessary to burden these pages with precise references to original papers. I have, however, on several occasions referred the reader to articles likely to be within his immediate reach.

Sixty new illustrations and a coloured frontispiece have been added. To these the increase in size is mainly due. Nearly all of them are from drawings or engravings by Mr. Collings, who has taken the utmost pains to ensure clearness and accuracy. Some of these replace less satisfactory illustrations in the last edition. In every case where specimens have been lent, I have acknowledged their source—in the case of those which have appeared in previous editions, by adding the name of the donor; and in that of specimens which appear for the first time in this edition, by a slightly longer and therefore distinguishing statement.

I gladly avail myself of this opportunity of acknowledging the help I have received. To my friends and colleagues, Dr. Mott, Dr. Arkle, and Mr. Stanley Boyd, I am indebted both for suggestions and

specimens. Dr. Mott has, in addition, contributed the chapter on Diseases of the Nervous System. I much regret that exigencies of space have prevented him from dealing more fully with the subject. In like manner, Mr. Boyd has written the section on Tubercular Diseases of Bones and Joints. For various items of help—specimens, drawings, blocks, or criticism—I am also indebted to Dr. Macfadyen, Dr. Manson, Dr. Rolleston, Dr. Ruffer, Dr. Sherrington, Dr. Woodhead, and Messrs. J. B. Lippincott Co. The *Index* has been prepared by my friend and demonstrator, Mr. Harold, who has also assisted me in the revision of the proof-sheets. I trust that Mr. Renshaw's good nature in carrying out all my whims in the matter of type, paper, and other details will be appreciated by the reader whose labour I have thus sought to lighten.

I can only hope that neither lack of knowledge nor defect of judgment on my part will in any way mar the reputation of this text-book, or stultify the confidence which Dr. Green, my predecessor in the Lectureship on Pathology at Charing Cross Hospital, has ventured to repose in me.

H. MONTAGUE MURRAY.

March, 1895.

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Pathology of the Central Nervous System.

By Dr. F. W. Mott.

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INTRODUCTION.

Anatomy and histology investigate the naked-eye and microscopic structure of the healthy body; physiology examines the functions of the parts revealed by them, and studies the chemical processes which constitute healthy life. To obtain a knowledge of disease, parallel courses must be adopted. At post-mortem examinations we note all the naked-eye departures from normal anatomy; with the microscope we discover the finer changes to which these departures are due; and by experimental methods and bedside observations we investigate the causes of the abnormal structure and function, their mode of action, and the nature and sequence of the disturbances which they produce. In other words, just as we have anatomy, histology, and physiology, so also we have morbid anatomy, morbid histology, and pathology.

Our guiding principle in modern pathology is that we have to deal not with new tissue-cells and functions, but simply with disturbances of ordinary elements and functions. It is obvious, therefore, that for the purpose of studying disease, our acquaintance with the body in health cannot be too intimate. New cells (bacteria) and even entire animals (parasitic worms) are frequently introduced into the tissues, but as *causes*, not *products*, of disease.

The complex human organism can be reduced to very simple elements—the *cells*, and the *intercellular substances* to which they give origin. These two elements make up every tissue. Sometimes the cells are in excess, as in the epidermis, where they seem to be in absolute contact; and sometimes the intercellular substance, as in the connective tissues. It is now universally believed that the individual *cell* is the seat of nutrition and function. Health and disease must be considered as terms referring, not to the body as a whole, but to the actual *cells* of which it consists.

Before treating of disease allusion must be made to the constitution of cells in health; as well as to their functions, and to the conditions under which these are normally discharged.

CONSTITUTION OF CELLS.—When Schwann established the analogy between the animal and vegetable cell the former was held to be constructed, in all cases, upon the same principle as the latter, and to consist, therefore, of a **cell-wall** enclosing a cavity in which were contained a **nucleus** and **fluid contents** (Fig. 1). But the fact that no cell-wall could be demonstrated in embryonic cells, blood-corpuscles, and the cells of many rapidly growing new formations, led Leydig and Max Schultze to believe that a little mass of matter, enclosing a nucleus, was all that was necessary to constitute a cell. Max Schultze established the identity of the cell-substance with animal sarcode—a contractile substance existing in the lower animals—and showed that it also was capable of spontaneous movement. He called this substance, of which all cell-bodies, animal or vegetable, are, at one period of their existence, composed, **protoplasm**; and pointed out that a distinct cell-wall resulted from a retrograde process occurring in its outer layers.

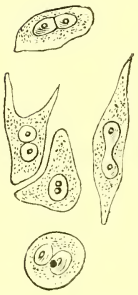


FIG. 1.—*Cells from a Cancer.* Showing cell-wall, cell-contents, nuclei, and nucleoli; the nuclei dividing.

The definition of a cell has been still further modified by the discovery that a nucleus is not essential; for none exists in the cryptogamia and in some of the lowest animal forms. In these exceptional cases the cell consists of a simple mass of protoplasm; but in the higher animals the nucleus is an almost invariable constituent. The cell-wall is much less constant, and must be regarded, in point of vitality, as inferior to the rest of the cell.

Protoplasm is a complex living body; of its molecular constitution we are still ignorant. It contains a large quantity of water, and its solid residue is largely made up of proteid material; but with this there are always associated, apparently in an amalgam-like way, some carbohydrate, fat, and inorganic salts—for these are invisible, and yet not in true combination. Some authorities regard the proteid element as alone essential to the manifestation of life. Protoplasm, as seen in the bodies of living cells, is generally structureless, soft and viscid, but varying much in fluidity. Granules are frequently present in it, often

in one part and not in another, and these are believed to differ chemically from true protoplasm. Small cavities, full of fluid, looking like clear spaces, are often seen; one large one may occupy a considerable portion of the cell, or many smaller ones may be distributed through it. These cavities are called *vacuoles*. They may appear, disappear, or change their position.

In highly specialised cells, protoplasm has acquired a distinct structure — *e.g.*, the fibrillation of muscle and nerve-cells and the striation of many ciliated cells and gland-cells. In the simpler cells, after hardening in chromic acid, a fine network of fibres is seen in the cell-substance, a fact which has led to the belief that the protoplasm of all cell-bodies is really arranged like a sponge; the interstices being occupied by fluid containing granules which are moved about by contractions of the protoplasm. This view explains many phenomena of cell-life; but, up to the present time, these appearances have not been observed in living cells.

Schäfer has recently shown that protoplasm is composed of two substances: (1) *spongioplasm*, which forms a reticular framework, and (2) *hyaloplasm*, which is structureless, semifluid, and not necessarily confined within the limits of the reticular framework. The movements of the cell depend upon those of the hyaloplasm. Butschli considers the structure of protoplasm is analogous to that of foam—"minute droplets of a watery liquid take the place of air in the bubbles of foam." He agrees with Schäfer in considering it reticular, but differs in his interpretation of what he sees, as well as in his observations on the arrangement and disposition of the framework itself. He thinks he can trace a reticular structure in the "processes," and that it fades gradually, in them as elsewhere, into the more liquid element. Schäfer thinks the limit is sharply defined, and that the pseudopodia are homogeneous.

Under certain circumstances protoplasm undergoes metamorphoses into various other substances—*e.g.*, mucin, globulin, keratin, pepsin and other ferments, glycogen, colloid matter and fat. These may form large portions of the bodies of cells. When glycogen and fat arise from a proteid, a nitrogenous molecule must also be formed.

This protoplasm is the essential constituent of the **body** of every cell. In comparison with the nucleus the body varies much in size, being sometimes large and sometimes quite insignificant.

The **cell-wall**, when present, is of much firmer consistence than the

rest of the body, and seems to be due to some metamorphosis of the protoplasm of the latter.

The **nucleus** is more constant than the body, both in size and form. It is usually spherical or oval, but may be quite rod-shaped: it is generally placed near the centre of the cell, and may be single or multiple. It resists destructive reagents more strongly than does the body, and in disease often remains after this has been destroyed; it is stained more deeply by carmine and logwood. Its presence may be concealed by fat, pigment, or other substances in the cell-body. The nucleus of epidermic scales may finally be converted into keratin and disappear.

The nucleus, which was formerly regarded as a spherical vesicle, bounded by a definite membrane which separated the nuclear fluid from the cell-substance, is now known to possess with great constancy the following much more intricate structure:—(1) A membrane bounding it externally; (2) a network of fibres, probably contractile, and certainly capable of great changes in closeness and general form; (3) one or more nucleoli, said by some to be only nodal points in the network; (4) a clear, more or less fluid, substance which fills the membrane and lies in the meshes of the network. The more solid portions—membrane, network, and nucleoli—are spoken of as chromoplasm or nucleoplasm; the less solid, as nuclear matrix. The remarkable changes which occur in nuclei previous to the division of cells will be described subsequently (p. 11).

PHYSIOLOGY OF CELLS.—In order to form an adequate conception of the changes which occur in disease, it is essential to remember the normal functions of cells and the conditions under which they are discharged.

A unicellular organism, like the amœba, takes in food, grows, excretes, reproduces its like, and performs certain functions, of which motion is the most obvious. The whole of this may be regarded as work done, and implies the expenditure of force; and we may be quite sure, although we know nothing of the chemical processes going on in an amœba, that its excreta are simpler compounds than its ingesta—the difference in heat-value between these two sets of compounds representing the force which is available to the organism. The ability to effect these chemical and physical processes, in which the "life" of the animal—as recognisable by us—consists, is inherited, and is spoken of as "*vital activity*," or "*vital energy*." The possession of

this is naturally the first essential to living. The other requirements of the cell are a *sufficient supply of suitable food* and an *appropriate physical environment*—such as a normal temperature, and suitable density of the surrounding fluid. To these must be added—in the case, at least, of nerves, muscle, and certain gland-cells in man—*connection with a healthy nervous centre.*

In man, a multicellular being, the cells vary much in form and in the results of the chemical actions which they effect. Although retaining more or less independence, varying with the kind of cell, they are bound together for the common good, and each has some special function to perform. Thus there are muscle-cells to produce motion, gland-cells to secrete and excrete, and nerve-cells to control the working of muscle, glands, and perhaps other tissues; certain cells are set apart for reproduction; and, finally, there are the connective-tissues to unite and support the other structures, and epithelium to protect the surfaces. Thus each kind of work done by the one cell of the amœba is in man performed by a group of cells specialised for the purpose. If then we recognise the inter-dependencies of the cells in the human organism upon each other, and the differences in their structure and purpose in the economy, all that has been said of the amœba will apply to each cell of the body—all the functions of the amœba are probably present in each cell, but one—*e.g.*, contractility of a muscle-cell, is often so highly developed as to be called *the* function of the cell.

Vital Activities.—The *vital energy* of each cell manifests itself in three channels; hence Virchow speaks of the *Nutritive, Functional,* and *Reproductive Activities.* Between the two former there is no line—the existence of one implies that of the other; both are chemical, and may be considered together. *Food* is taken into the body, digested, and absorbed by lacteals and blood-vessels from the intestines; the various excretory organs give off urea and, in small quantity, other nitrogenous bodies, carbon dioxide, and water. Supposing the body to be in *nutritive equilibrium*—neither gaining nor losing weight—the amounts excreted will account for the nitrogen, carbon, and hydrogen taken in as food. Putting aside water, certain salines, and oxygen, which are essential to life, the food-stuffs are proteids, carbohydrates, and fats—the materials of which the body consists. It is evident that a large amount of heat must be set free in the breaking-down of these bodies into the simpler substances above mentioned. This is the source of the force by which every act is performed. The blood

carries the prepared food-stuffs to the capillaries, whence they pass out with the lymph to come into actual contact with the cells—some in solution, others only in suspension. Certain, or all, of these bodies are now taken up (apparently actively, for albumen will not diffuse from a watery fluid), and become *part of the substance* of a cell, replacing some older material which has been broken down to supply force for assimilation and all other actions of the cell. This breaking-down of cell-substance consists in the union of it with oxygen obtained from the blood, and stored by the tissues in some unknown way. All such oxidation processes are believed to take place *in the cells, not in the blood;* and this almost necessitates that all food shall become part of a cell before it is oxidised; it is not oxidised directly. Although the tissues of the body and the food-stuffs have almost the same chemical composition, waste tissue is not repaired by a process of simple replacement from the food, if we except fat: when a fat of the same composition as human fat is contained in the food, it may be stored in the cells without undergoing previous change, but usually some slight addition or subtraction of hydrogen is necessary. It is probable that many changes, both analytical and synthetical, occur in the arrangement of the elements of food-stuffs before they form protoplasm, the real *living* tissue, and force is thus alternately liberated and rendered potential; but this does not affect the main fact that the body is ultimately enabled to utilise the force equivalent to the difference in heat-value between the ingesta and excreta.

We have enumerated the compounds presented to cells in lymph, and also those which leave the body as the ultimate products of cell-action; but in no instance do we know the connecting links between the end-products. Whilst the ingesta of cells must be tolerably uniform in character, their excreta are probably as various as are the uses of the cells in the body—witness the different compositions of the many secretions, and the unequal distribution of the extractives, such as kreatin and xanthin. On the one hand, the breaking-down of tissue, or *waste,* which is going on constantly, and on the other, the building-up, or *repair,* which in health keeps pace with it, constitute the *nutritive exchange* of the cell or of the whole body. This process is constantly being disturbed from pathological causes; and, physiologically, formation exceeds waste during the period of growth, but the opposite obtains in old age, when the vital energy of all cells is failing, and their functions are imperfectly discharged.

The excreta pass in two directions: into lymph and back into the

blood, or out to a mucous or cutaneous surface, whence part may be re-absorbed, *e.g.*, saliva, gastric juice, and part of the bile.

Influence of the Nervous System on Nutrition.—Experimental physiology teaches us that the nervous system has an important influence over the nutrition and function of nerves, muscle, and such glands as act normally only in response to the stimulation of special nerves. Thus when motor nerve-fibres are cut off from the ganglion-cells of the corresponding anterior cornu, they rapidly degenerate and lose their power of transmitting electrical as well as voluntary impulses. The muscles they supply also undergo degeneration (p. 56), and show changes in their electrical reactions. In the same way section of the chorda tympani is followed by wasting of the sub-maxillary gland.

It is at present uncertain whether the nervous system has any analogous influence over other tissues, such as connective-tissues and epidermis, for while lesions of these structures are frequently found associated with disease of the nervous system, it is in all cases difficult to exclude other possible causes. Thus these lesions are accompanied by more or less anæsthesia, disturbance of the circulation, and fall in temperature; all of which may be actively concerned in the causation of the subsequent changes. For example, in inflammation of the peripheral nerves, such as occurs in chronic alcoholism, not only do the nerves and muscles undergo the changes just mentioned, but the skin supplied by the affected nerves frequently becomes thin and shiny; moreover, bullæ not infrequently appear.

Occasionally in cases of hemiplegia, and of sabre-wounds of the brain, extremely **acute bedsores** form on the buttock opposite the lesion; and similar lesions may appear over the sacrum in paraplegia from sudden and extensive lesions of the cord. They are distinguished from ordinary bedsores by the earliness (second or third day) and acuteness of their onset, and by the uselessness of precautionary measures. It may be replied: that these are but differences of degree; that the bedsores occur in the usual positions; and that apparently similar lesions show, in this respect, no proportionate constancy in their results. In this class of cases, too, **cystitis** and **pyelitis** may appear at about the same time as the bedsores, and Charcot thought that these inflammations were due to irritation of trophic nerves; but as exceedingly foul urine, containing organisms, is noted before, or with, the onset of the cystitis, others believe that these changes are due to the organisms—either introduced from without by a septic catheter; or from within, through

the kidneys. The urine is thus rendered extremely irritant by putrefaction. Similar results occasionally follow the passage of a catheter in cases of enlarged prostate.

Trigeminal Keratitis.—Intra-cranial section of the fifth nerve causes cloudiness of the cornea in twenty-four hours, and often destructive panophthalmitis; at the same time ulcers appear on *insensitive* parts of the mucous membranes of both mouth and nose. The keratitis can be prevented by carefully cleansing and accurately closing the eyelids, thus protecting the parts from organisms and injuries. The ulcers in the mouth are probably due to damage inflicted by the teeth, and the ulcers in the nose to the action of particles of dust and organisms on the dried mucous membrane. In both cases the failure of the insensitive mucous membrane to initiate any of the vaso-motor and other protective reflex mechanisms renders the parts a suitable culture ground for passing organisms which are thus enabled to thrive on the insensitive surfaces. **Ulcers on the foot,** often progressive, after section of the sciatic are similarly accounted for.

Acute fatty degeneration of the heart may follow section of the vagi: the *modus operandi* is unknown.

Erythema, Urticaria, Pemphigus, and especially **Herpes**, may appear in the distribution of nerves, which are the seats of some irritant lesion. These changes have been observed after fractured spine, in locomotor ataxy, in syringomyelia, in compression of the cord by an aneurysm or tumour, and in inflammation of the Gasserian or some posterior spinal ganglion. The nerves supplying the area of the rash have been found in a state of neuritis.

Glossy Skin (Paget).—In some cases of irritative lesion of the sensory nerves of limbs (*e.g.*, from gun-shot), the skin becomes smooth, shiny, hairless, sometimes hyperæmic, sometimes œdematous, and often superficially inflamed or the seat of sores like chilblains; at the same time the part is often the seat of intense neuralgia. All these changes in the nutrition of the skin are probably due to vaso-motor changes acting in conjunction with external influences such as have been mentioned above.

Pigmentation.—More or less symmetrical patches of leucoderma and melanoderma may be distributed over the body, with more or less anæsthesia. Pallor with anæsthesia and localised greyness of hair may occur in neuralgia of branches of the fifth nerve. The colour of the hair may to some extent return between the attacks. Cases have

been recorded in which the hair has, within a short time of a fright, become grey.

Serous Synovitis, and **Arthritis** with rapid, painless, and extensive erosion of the articular ends of the bones, may occur in cases of hemiplegia and locomotor ataxy. These are supposed to be due to involvement of the cells of the corresponding anterior cornu by progressive atrophy. The causal relationship between the nervous disease and the peripheral lesion cannot yet be said to be proven.

Atrophy of parts cut off from the nervous system.—Muscle and certain glands have already been referred to (p. 7). In the case of muscle, it is to be noted that if it is regularly exercised by the galvanic current, atrophy may be postponed. In a paralysed limb all tissues ultimately waste; so, also, do those of the face when the facial nerve remains paralysed. This is due to impaired blood-supply, for it occurs in limbs which are simply kept at rest. Atrophy of the cock's comb and the turkey's wattles results from section of their nerves, and is perhaps to be similarly explained. In cases of progressive atrophy of half the face there may be nothing to guide one to the nervous system as the cause: there may be no subjective symptoms, and sensation and motion may remain normal. If due to nervous influence, this atrophy would seem to favour the existence of trophic nerves.

Hypertrophy of bone may follow section of the sciatic in young animals, and is inflammatory; for it never occurs unless large ulcers form, extending to the bone, and even causing necrosis. Hypertrophy of the rabbit's ear after section of its nerves has been said to occur; but many observers have failed to produce the hypertrophy, or have, at most, seen some thickening of epidermis and hair upon the surface of the ear.

Pathology, then, affords *no reliable evidence* of the existence of special trophic nerves, and no convincing proof of the interference of the nervous system in the chemical processes of cells which perform no special function. That these processes may go on undisturbed in the absence of nervous influence is shown by the perfect development of other parts which is found in anencephalous and amyelous embryos; by the growth of transplanted epithelium and connective-tissues, and by the union of completely severed parts. At the same time, as we cannot offer a perfect explanation of many of the above-mentioned cases, we cannot say that the nervous system has no direct influence upon connective-tissues and epidermic cells—it seems most probable

that it has. It is important that the facts should be remembered. The explanation of some of them is at present uncertain.

The *Reproductive Activity* remains for our consideration. In early life, at least, all cells possess the power of reproducing their like, and in the majority this power is retained, although it may not be exercised physiologically, up to advanced age. Cessation of growth does not imply absence of ability to grow, for growth sometimes seems to cease when the supply of nutritive material to a part is only just sufficient to maintain its *status quo*. This is seen in a hair, which will not grow beyond a certain length—cut it short and growth at once begins again, the supply of food being greater than the now shortened hair requires for simple nutrition. To cause cells, which are capable of multiplying, to do so, the supply of food must be increased. Thus exercise of a muscle causes increased blood-supply and consequent growth; but increased blood-supply to a working tissue, without exercise, will not have this effect. It is different with non-working tissues. The hyperæmia round an ulcer of the skin causes thickening of the epidermis and connective-tissues, and nothing is commoner than new formation of bone round a carious focus. To produce this effect the increased supply must be very frequent or long-continued (see "Ostitis").

A non-working tissue apparently tends to grow also when the resistance offered to its growth by neighbouring tissues is diminished: of this we shall find many examples in cirrhotic processes and in the ætiology of malignancy (Cohnheim).

The cells of the body inherit very different amounts of vital energy. The cells of the thymus are soon exhausted, those of the epiphyseal cartilages later, and of the generative organs later still. Powers of maintenance, growth, and reproduction are by no means proportionate. The power of reproduction possessed by cells often seems inversely proportionate to the specialisation of their function (p. 101). In all cases, probably, the reproductive activity is the first of the vital manifestations to suffer; then the functional and nutritive. Inability to perform such chemical changes as are necessary to remove effete material and to repair waste is normal in old age; death, which may be termed natural, then results from "senile decay."

GENESIS OF CELLS. — Virchow's dictum — *Omnis cellula e cellula*—is now admitted by all but a few. Probably every nucleus, also, is derived from a pre-existing nucleus.

Multiplication of cells takes place by **simple division**. The cell divides generally into two ; and the change is preceded by remarkable appearances in the nucleus. According to Flemming the process of "karyokinesis" may be very briefly described as follows (Fig. 2) :— First, the *nuclear membrane* disappears ; then the *resting* nuclear network (*a*) becomes much finer and closer, like a ravelled *skein ;* then again more open, and, if not already so, the cell becomes round (*b*). There seems to be now only one long fibre forming the nuclear network,

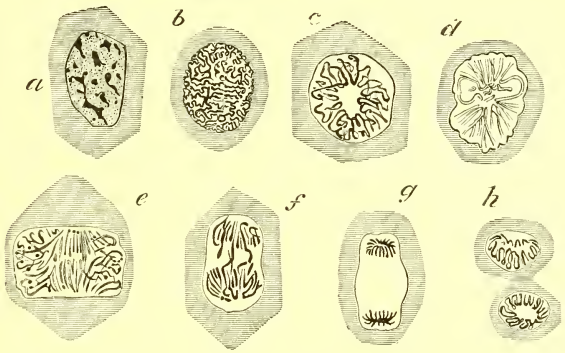


FIG. 2.—*Forms assumed by a Nucleus in dividing*—*a*, resting nucleus ; *b*, skein-form, open stage ; *c*, wreath-form ; *d*, aster, or star-form ; *e*, equatorial stage of division ; *f*, separation more advanced ; *g* and *h*, star and wreath forms of daughter nuclei. (Reduced from Flemming's drawings in the "Arch. f. Mik. Anat.").

which next assumes the form of a *rosette* or *wreath* (*c*), round a clear central space, whilst a clear zone intervenes externally between the network and the cell-substance proper. By division of the external bends of the fibre, and approximation of the apices of the V's so as to obliterate the central space, a star-form—*aster* (*d*), is produced. The fibres at this stage often become finer and more numerous by longitudinal division from their free ends towards the centre. Instead of radiating from the centre they now become first parallel, and then convergent towards two opposite points—the poles—of the original nucleus, so that the fibres now form two sets of V's with their angles away from the equator—**equatorial stage** (*e*). A clear equatorial line appears, and widens (*f*), as one set of V-fibres retreats from the

other. From each group the nucleus of a daughter-cell is formed by passing through—in reverse order—all the stages above-mentioned (*g* and *h*), until the resting stage is reached. Meanwhile, the protoplasm of the cell-body collects round each nucleus, and by the time these have assumed the wreath-form its division is complete. The daughter-cells, at first small, grow, and may themselves soon divide; thus multiplication may be very rapid.

The nucleus may divide several times without any division of the cell-body occurring; but the latter increases continuously in size. This is said to be one way in which "giant" or "myeloid" cells—large, irregular, multinucleated masses of protoplasm, found in the marrow of growing bone, in chronic inflammations, and in some new growths—may be produced (Fig. 3).



FIG. 3.—*A Multinucleated Cell.* From the lung in a case of Chronic Phthisis. Showing the large number of nuclei with bright nucleoli. × 400.

Finally, it remains to be pointed out, that cells originating from one embryonic layer never give rise to cells of a kind formed normally from another layer. **Epiblast** forms nervous tissue, and the epithelium of sense-organs, of the ventricles of the brain and central canal of the cord, of the skin, mouth, and lower end of rectum. **Hypoblast** forms the epithelium of the urinary bladder, respiratory tract, and alimentary canal and of all glands connected with it. The **Mesoblast** forms the epithelium of the kidney, testicle, and ovary; the epithelium of vessels and serous membranes; all the connective-tissues; blood; and muscular tissue.

DISEASE.—The functions of an organ are really the functions of the cells of which it consists; if all these act normally we say that the organ is sound; and when all the functions of every organ and tissue in the body are normally performed, we describe the individual as being in perfect health. A very little experience shows that physiological functions vary within certain, perhaps rather wide, limits, the perfect well-being of the individual being maintained. Consequently our standard of **Health** is no rigid one; its maximum and minimum

are widely separated, and the latter shades off imperceptibly into **Disease.**

Disease may therefore be defined as *the abnormal performance of function by one or more organs or tissues.* This applies to "disease" as a general term; but when we speak of an individual disease, as rheumatism or syphilis, the *cause* of such disease—that to which the peculiar disturbances of function or structure, which distinguish the disease in question from all others, are due—is often implied in the word. The same, or indistinguishable, disturbances of function and structure, may sometimes be produced by several causes: it is the more or less constant grouping or sequence of symptoms or of lesions which in such cases establishes distinct diseases.

It is worthy of note also that the *maintenance of a physiological maximum or minimum* must be regarded as pathological. For example, a man out of training will eliminate much more urea than normal on the first day of a walking tour, but the average daily elimination for the whole tour will not vary from the normal. If, however, the man were to go on excreting the maximum quantity of the first day, his state would be one of disease.

VARIETIES OF DISEASE.—The complete healthy life of a cell consists in the perfect performance of all its functions. For this, three things are necessary:—1st, that which it inherits—its vital energy—must be normal; 2nd, it must be supplied with sufficient suitable food; 3rd, its surrounding physical conditions must be normal. Failure in any one of these will lead to disease, and two great classes of diseased conditions are at once evident—**inherited**, due to abnormality of the first; **acquired**, due to abnormality of the second and third.

Inherited Disease.—The tendency to inherited disease either exists in the ovum at the commencement of development, or is acquired by the ovum in fertilisation: tendencies formed later than this are obviously acquired. As in normal development certain organs manifest their inherited tendencies many years after birth—*e.g.*, the development of the female generative system at puberty and its atrophy at the menopause; so inherited tendencies to disease may not show themselves until late in life, as is the case in cancer of the breast or uterus. It is possible that in many cases the same unrecognised conditions which induced in a parent the morbid tendency handed down, continue to act on the offspring, until—with or without

some obvious exciting cause—the disease becomes evident. We cannot say when this tendency to disease begins: it may have been slowly gaining strength for generations. The fact that no progenitor had the disease in question, if he or she lived well past the age at which such disease usually manifests itself, shows simply that the causes had not acted long enough or with sufficient energy to produce it. It is important to recognise that even inherited disease has its starting-point in conditions external to the cells of the body.

With regard to the actual mode in which disease is inherited—it is in some cases probable that the poison, the actual cause of the disease, is present in the ovum or spermatozoon, as has been shown to be the case in the silkworm disease (Pasteur). But how disease and tendencies to diseases which are not due to any specific poison are handed down, we know no more than we do how it is that children inherit the features of their parents.

Often, no actual disease is inherited, but the power of resistance of certain tissues against the causes of certain diseases (*e.g.*, tubercle) is more or less impaired; or the tissues degenerate early, especially in the fatty or calcareous manner, so that many members of a family may die at about the same age from fatty heart or apoplexy.

Acquired Disease.—Starting with an organism or part possessed of normal vital energy, disease, if it occur, must necessarily be the result of external conditions; the supply of food is faulty either in quantity or quality, or the physical conditions to which the part is, or has been, exposed are unsuitable. It is difficult to separate the two. If the blood-supply to a part is abnormal in quantity, the temperature of the part will be changed; if a portion of the body is mechanically injured, its blood-supply becomes abnormal; if a poison excites fever, the cells are exposed to a higher temperature than normal: a *circulus vitiosus* is established. Disease may be acquired even during intra-uterine life—*e.g.*, one of the acute specific fevers, or syphilis.

General and Local Disease.—Any change in external conditions acting upon a unicellular organism would probably affect every particle of its substance and modify all its functions; all its diseases would therefore be **general**. But multiplication of cells and specialisation of functions enable abnormal conditions to act upon certain groups of cells and to disturb their functions without affecting—primarily, at least—those of other groups. We thus get **local** disease; and the great majority of diseases belong to this class. Perhaps, indeed, we may say that every disease is primarily localized in a tissue or organ—

the blood being counted as of the connective-tissue type of which the intercellular substance is fluid.

Structural, Organic and Functional Disease.—A disease is localized in an organ or tissue during life, by its symptoms and by its physical signs; and after death, the localization is justified by the discovery in the part of some constant structural change. This is **structural** or **organic** disease. Diseases, in which no such change has been found, or is believed to exist, are classed as **functional**; the belief being that in them the functions of certain cells are abnormally performed, without any structural change. Modern research has greatly diminished the number of functional diseases; but it is almost certain that a very large number of the slighter ailments are due to transient errors in the metabolism of the cells.

ÆTIOLOGY OF DISEASE.—The causes of disease are divided into two classes—**Predisposing** and **Exciting**.

Predisposing Causes.—Any agency which tends to cause departure from the physiological condition of a function, must be regarded as predisposing to disease—*e.g.*, privation, and frequent irritation. Many such agencies, when acting more strongly, become excitants of disease—*i.e.*, cause a departure *beyond* the physiological limit. Thus if to normally acting ciliated cells, detached from the body, a hot iron be approached, the first effect will be to increase or stimulate the movement of the cilia; but if the iron be kept near them long, or be brought closer, the movement becomes slower and soon ceases. If the iron be then removed, the cilia will after a period of quiescence begin to work again—at first one here and there, then all—and may after a time recover completely. This experiment of Lister's illustrates a point of fundamental importance in pathology—*the inherent power of every cell to recover after injury.* It shows for the elements what every one knows of the whole—namely, that, *cæteris paribus*, a strong man will recover from a disease which would be fatal to a weakly one. It is certain, too, that the "life" of cells resists the action of injurious agencies; and that this power of resistance varies both in the case of different *tissues*—*e.g.*, the rabbit's ear resists the effects of anæmia much longer than a knuckle of its intestine—as well as in different *individuals*. Thus it is a common observation that certain people, who have not suffered from the acute specifics, may even nurse those ill of these diseases without themselves catching them; whilst others again fall

victims to them, though not specially exposed. Such power of resisting certain causes of disease does not imply ability to resist others of a different nature; nor does it necessarily go with muscular strength. It varies at different times in the same individual.

The following may act as predisposing causes:

Age.—Special treatises have been written on diseases of childhood and on diseases of old age, showing that there are peculiarities with regard to disease at these periods of life. The special liabilities of childhood are to some extent explained by supposing that the power of resisting injury, which all cells possess, is not fully developed until adult age; those of old age, by the fact that the vital powers are wearing out, and degeneration occurring.

Sex.—The organs special to the sexes render each liable to special diseases. Women are the special victims of hysteria and chlorosis. We cannot explain the special liability of women to endemic and exophthalmic goître and to myxœdema, nor their comparative immunity from Addison's disease, locomotor ataxy, and general paralysis.

Heredity.—It has already been stated that feeble vital power, without actual disease, may be the heritage of the body, or of one of its parts. It may further be noted that, like physiological and personal peculiarities, disease, *e.g.*, gout, sometimes skips one or more generations (*atavism*). In other cases, as in hæmophilia and pseudo-hypertrophic muscular paralysis, the disease appears generally in the males only; although the females may, without themselves manifesting it, transmit it to their offspring.

The diseases which most obviously "run in families" are:—functional nervous disorders, such as hysteria, neuralgia, epilepsy, insanity, and these are more or less interchangeable; carcinoma, especially of the breast and uterus; some simple growths, especially if multiple (lipomata, osteomata, papillomata); gout and tubercular disease.

Exciting Causes.—These may be arranged under the headings of *Abnormal Blood-supply and Abnormal Physical Conditions;* it may be necessary to add, *altered nerve-influence,* but we do not as yet know enough about it.

Abnormal Blood-supply.—Defects in the blood supply may be due to errors in the circulation or in the composition of the blood. It may result from hyperæmia or anæmia; from all abnormalities in blood-constitution, whether due to faults in its formation or purification, or to the introduction of poisons or parasites from without.

Abnormal Physical Conditions.—This group includes injuries from any one of the physical forces, applied either from without, or, so to speak, from within; also the results of mechanical obstacles to discharge of function or of contents—*e.g.*, stricture of a duct or orifice, strangulation of gut, pressure, and the mechanical effects of parasites.

EFFECTS OF PREVIOUS DISEASE.—Some diseases, when they have occurred once, tend to recur again and again. In the case of others, to have suffered once is to have secured practical immunity against a second attack (see "Immunity").

Certain other diseases, again, seem to modify very deeply the functions of the body. Many years after these diseases, it is found that illnesses, which seem at first sight to have nothing to do with them, yield only to the treatment proper for the original malady. Such are malarial fever, syphilis, and gout. The poisons of the first two are probably still latent in the body: as to gout, we know too little of its essential nature to speak definitely of the way in which its influence is exercised.

MODES OF EXTENSION OF DISEASE.—**Primary** disease of an organ or tissue is frequently followed by **secondary** disease of other parts. This may happen in several ways:—

1. **By direct spread of a morbid process**, as when inflammation extends from skin to subcutaneous tissue, or when cancer of the mamma invades the superjacent skin.

2. **By the carriage of the causes of disease from a primary focus to parts at a distance.**—Thus organisms may be carried by the *lymphatics*, and give rise to inflamed lymphatic glands; pieces of clot may be conveyed by the *blood-vessels*, and produce embolism; and a renal calculus may be transferred through the ureter to the bladder.

3. **Mechanically,** by so-called "*back-telling.*" Thus stricture of the urethra causes hypertrophy of the bladder to overcome the obstacle to the outflow of urine, or dilatation of the bladder if its efforts are futile. In either case, the difficulty of entry of urine into the bladder is increased, and the ureters, pelves, and kidneys dilate. Interstitial nephritis results from the pressure, the renal functions are imperfectly performed, and this is detrimental to the organism at large. The succession of changes which result from mitral incompetence is another familiar example of this mode of extension of disease (see "Mechanical Hyperæmia").

4. **Failure of any part to do its share of work in the economy.**—The result of such failure will depend upon the readiness and completeness with which its defection can be compensated. If the work can be readily taken over by other parts, as can that of a sweat or sebaceous gland, nothing is noticed; on the other hand, extirpation of a kidney which was doing work, is followed by a time of danger from diminished excretion of urinary products, as the other kidney is at first unequal to the double duty. Absolute failure of the cardiac or of the respiratory function will cause death, there being no power of compensation.

TERMINATIONS OF DISEASE.—The possible terminations of disease are *recovery,* or return of the part to the discharge of its normal functions; *partial recovery;* and *death,* or complete cessation of function. Certain diseases can scarcely be said to have a termination; when once established they remain stationary.

It will be useful here to give a list of the morbid processes to which all organs are more or less liable:—

The results of mechanical or physical injury.
Displacement.
Hæmorrhage.
* * *
Developmental errors.
* * *
Anæmia.
Hyperæmia.
Œdema.
Inflammation.
Atrophy.
Degeneration.
Necrosis.
Regeneration
Hypertrophy.
Tumour-formation.
* * *
Lodgment of parasites.
* * *
Stricture and its consequences may occur in every duct or canal; and calculi may develop in any of them.

CHAPTER I.

NUTRITION ARRESTED.

Necrosis.

The complete and permanent arrest of nutrition in a part constitutes necrosis, gangrene, or local death.

ÆTIOLOGY.—Whatever interferes with the supply of nutritive material to a part, or destroys the vital activity of its cellular elements, may cause its death.

A. Interference with the Supply of Nutritive Material.—Such interference may be the result of:

1. **Obstruction in the Arteries.**—This is a common cause of necrosis. The obstruction may be caused by compression, by ligature, by rupture, by thrombosis, by embolism, or by disease producing thickening of the arterial coats. If the obstruction be complete and a collateral circulation cannot be established, death of the part quickly ensues.

2. **Obstruction in the Capillaries.**—Obstruction is often the result of pressure upon, or stretching of, these vessels. This may take place from the accumulation of inflammatory products, or of extravasated blood, or from the pressure exercised by new growths. The resulting obstruction to the capillary circulation causes the death of the immediately adjacent tissues. As examples of necrosis from this cause may be mentioned: necrosis of the superficial layers of the bone resulting from periostitis, and due to the compression of the capillaries between the bone and the periosteum; the sloughing of tendons in whitlows before the latter are opened; and the formation of ordinary bedsores. When inflammation causes gangrene it is by the production of stasis, leading to death of the tissues from malnutrition and coagulation of blood in their capillaries. Whenever necrosis of a tissue occurs, the blood coagulates in its capillaries; and thus hæmorrhage from gangrenous parts is prevented.

3. **Obstruction in the Veins.**—Obstruction to the return of blood by the veins must be so complete in order to arrest nutrition that it is in itself rarely a cause of necrosis. It is when associated with cardiac weakness or obstruction in the arteries that it constitutes

an important agent in producing this result; for then the force necessary to drive the blood on through the much narrowed venous channel is quite inadequate. Gangrene due to these combined causes occurs after ligature of a main artery and its vein, and may follow accidental injury of the vein during the operation of ligature of a large artery, especially in the thigh. It may also result from constriction of a part by a bandage not tight enough to occlude the arteries as well.

4. **Diminished Cardiac Power.**—This is never by itself a sufficient cause of necrosis. In cases, however, of excessive general debility, or of disease of the cardiac substance, the consequent diminution in the contractile power of the heart materially aids the foregoing causes in producing a fatal blood-stasis. The arrest of the circulation in "senile gangrene," and in that form which so often occurs in the tissues of the back in adynamic fevers and in chronic exhausting diseases, is in part the result of diminished cardiac power This arrest in the last-named conditions is usually determined by some injurious irritation of the tissue—in other words, it is a part of an inflammatory process.

5. **Inflammation.**—As a cause of necrosis, inflammation belongs partly to the group we are now discussing and partly to that on the next page; for the effect of the inflammatory process is to impede or arrest the circulation, as well as to impair the vitality of the affected part. The intensity of the process may be so great as to cause coagulation in the capillaries and death of the tissue. It is then called *coagulative* or *coagulation necrosis* (p. 22). When a strangulated or invaginated piece of gut is released and the circulation is re-established, severe inflammation, perhaps leading to gangrene, frequently ensues. Cohnheim's experiment of tying off a rabbit's ear has, in effect, been repeated (see "Embolism"). It is of practical importance to note that *inflammation* sets in only on *re-establishment* of the circulation, that is when the gut is returned to the peritoneal cavity: there is none whilst it is in the sac. A much contused and lacerated part may ultimately be killed because the pressure of the effusion from its injured vessels still further impedes the flow through them. Certain inflammations have a special tendency to terminate in necrosis, such as diphtheria, carbuncle, noma, "hospital gangrene," and spreading traumatic gangrene. In these conditions the intensity of the injury to the tissues is probably due to the action of minute organisms. In all cases, the more impaired the nutrition of the part which becomes

the seat of an inflammatory process, the more likely is the inflammatory process to cause its death.

B. Destruction of the Vital Activity of the cellular elements may be caused by :

Physical and Chemical Agencies.—A part may be completely disorganised and lose its vitality as the result of external violence, excessive heat, or extreme cold. Many corrosive chemicals, as acids and caustic alkalies, destroy the life of cells. Putrid urine or foul secretions from wounds will sometimes destroy the cells like a caustic. As implied in the last paragraph other organisms as well as those of putrefaction may produce a similar result. These physical and chemical agencies frequently cause necrosis by exciting, in the first place, acute inflammation.

These are the several causes of necrosis ; but it must be borne in mind that the process is often complex, and due to the combined influence of two or more of them. The liability to necrosis will greatly depend also upon *the power of the tissues to resist injury.* This varies, probably, in different individuals, and, certainly, in different tissues in the same individual—intestine, for example, being much less resistant to injury than skin. Conditions which would lead to the death of a part in which the circulation was already impeded, or in which the vitality of the cellular elements was impaired, would produce no such effect where such local weakness did not obtain. This is well exemplified by the necrosis of the tissues of the back from pressure, which so often occurs in conditions of debility ; by the formation of ulcers near varicose veins in the legs ; by the gangrene of the extremities which sometimes results from the long-continued ingestion of ergot ; and especially by senile gangrene.

THE CHARACTERS OF THE DEAD PART.—These generally resemble one of two types known as **dry** and **moist** gangrene respectively. There are three conditions which mainly determine into which of these two varieties a given instance will fall. These are (1) the amount of fluid which the involved tissues naturally contain ; (2) the extent to which the vessels of the part affected are engorged with blood, and the amount of fluid which is therefore present at the time ; and (3) the rapidity of the evaporation from the surface.

Dry gangrene will therefore occur in those parts in which the tissues naturally contain but little fluid, such as bone, cartilage, and tendon. It will also be frequently associated with such obstructions of

the arteries as may occur without any corresponding interference with the circulation in the veins and lymphatics. Dry gangrene, therefore, may result from embolism, from slowly progressing arterial thrombosis, and from the prolonged administration of ergot. Again, free exposure to dry air, slow progress, and the destruction of the epidermis will all, by promoting or permitting evaporation, aid in producing dry gangrene. Under these circumstances, the part, which is pale from the first, gradually dries up and becomes converted into a dark, shrunken mass, undergoing but little further change. The conditions obtaining in dry gangrene are precisely those which render the growth of organisms almost impossible.

Moist Gangrene.—Under opposite circumstances, a part, consisting largely of muscle and other soft structures may become rapidly gangrenous, either from an acute inflammation, or from venous obstruction combined with a weak arterial supply. When this happens its tissues are accordingly gorged with an albuminous fluid full of breaking-down red blood-corpuscles. The hæmoglobin of these forms a red solution which soaks into and stains all the tissues. The limb is much swollen, of purplish colour, and often studded with bullæ of blood-stained fluid. If such a part is exposed to warm, moist air, septic bacteria quickly enter through the skin, multiply rapidly in the highly putrescible fluid, and generate by their action gases—chiefly sulphuretted hydrogen, ammonia, nitrogen and carbon dioxide—which give rise to the emphysematous crackling so often associated with gangrene. The tissues soften and liquefy, the whole part becomes exceedingly offensive, and its tissues change in colour from reddish to brownish or greenish black. For putrefaction to occur it is absolutely essential that septic bacteria be admitted to the part; consequently such changes are met with chiefly in external parts or in those internal parts to which organisms have free access.

When the life of an internal organ or part is destroyed and bacteria are not admitted to it, as in simple infarction, its tissues undergo a series of degenerative fatty changes known as **necrobiosis.**

Coagulation necrosis is a term applied to a peculiar form of sudden tissue-death. The cells in dying seem to give rise to some substance or substances which unite with the lymph and cause an apparent coagulation of the dying cells. Microscopically, the nucleus disappears, and the contents of the cell are replaced by a structureless hyaline looking material. Fatty degeneration subsequently sets in. The process may be the result of bacterial action. It only

occurs in parts freely supplied with lymph, and is never found in the brain.

COURSE.—Gangrene may be **circumscribed** or **spreading**. The course varies chiefly with the *cause;* but the *resistance* of the tissues, which depends upon their vital energy and blood supply, must always be taken into account, for causes which have little effect on healthy tissues may lead to sloughing in the aged, in the diabetic, in the albuminuric, and in the intemperate.

With regard to the first factor—circumscribed gangrene implies a circumscribed cause. This form is exemplified by the death of tissue resulting from mechanical violence, the actual cautery, or complete stoppage of the circulation. On the other hand, spreading gangrene necessitates a cause which spreads before it. Thus gangrene from arterial thrombosis often spreads but slowly, and with a well-defined margin. But the typical spreading gangrenes are those due to inflammation, in which, probably, the action of organisms on the fluids of the part constantly provides fresh quantities of the irritant.

When the process becomes circumscribed, the dead tissue—*sphacelus* or *slough*—acts as an irritant to the adjacent living structures, causing more or less inflammation of them. If the slough is aseptic, the inflammation is slight—leading merely to the formation of a layer of fibroid tissue round the dead mass by which it becomes encapsuled. This occurs especially in internal parts, and is best illustrated by the fate of simple infarcts. When thus encapsuled the dead part ceases to irritate; it becomes decolorised, fatty, infiltrated with small round cells which absorb the fatty detritus, and ultimately converted into a small fibrous scar, which may calcify.

When the slough is superficial it generally putrefies and becomes strongly irritant; but mummification will minimise this. The inflammation of living tissue round the now limited slough is spoken of as the **line of demarcation.** Exudation and migration occur freely into a narrow zone of *living tissue* surrounding the edges and base of the slough; fibres and all firm connections between the living and dead tissues are softened and eaten through; and, finally, when this process is complete, the slough is cast off by suppuration occurring along the line of demarcation. If the whole thickness of a limb die, the stump left by casting off the sphacelus will be conical; for the soft parts retract somewhat, and the bone separates lower down. The less vascular a tissue, the longer will be the time occupied in its erosion—*e.g.*,

fascia, tendon, bone. If the dead mass be deeply seated, and suppuration occur about it, fistulæ will form, leading from it to the surface. Through one or more of these, it may ultimately be cast off, as is seen in necrosis of bone. After removal of the slough, an ulcerated surface is left.

Senile Gangrene.

This is a form of necrosis which affects especially the lower extremities of old people, and is the result of several of those ætiological conditions which have already been enumerated.

The most important element in the production of senile gangrene is the presence of *atheromatous or calcareous changes in the arteries* of the limb, which greatly diminish their elasticity and calibre, and proportionately impair the circulation in and nutrition of the part. This is shown by the coldness of feet, cramps, and other abnormal sensations so often experienced by the patient for some time before the gangrene sets in. The slowing of the circulation is usually much increased by defective action of the heart due to atrophy or degeneration of its muscular substance. Thus the contact of the blood with an abnormal vessel-wall is prolonged, and this is sometimes sufficient to cause the formation of a thrombus in the artery. The clot thus formed slowly spreads until it may extend from the foot to the groin. Gangrene then supervenes. It begins in one or more toes simultaneously and extends slowly. It is often surprisingly limited; and even where the thrombus extends into the popliteal artery, part of the foot may escape. In other cases *embolism* with superadded thrombosis, may be the starting point—a chalky plate or a parietal thrombus being swept from a large into a smaller artery.

Finally, the gangrene may be *inflammatory*, due to some trivial injury, such as a slight abrasion of the foot, the cutting of a corn, or some excess of heat or cold, acting upon feebly nourished tissues supplied by diseased vessels.

Fat Necrosis.

Under the name of *fat necrosis* a peculiar change occurring in fat has been described. It consists in the formation of opaque white areas, half an inch or less in diameter. These are of firm consistence, and are scattered through otherwise normal fat. They stain with osmic acid, and melt on the application of heat. Under the microscope the

contents of the affected cells are either crystalline, or opaque and granular. The transition from diseased to healthy cells is abrupt. The surrounding parts are occasionally infiltrated with small round

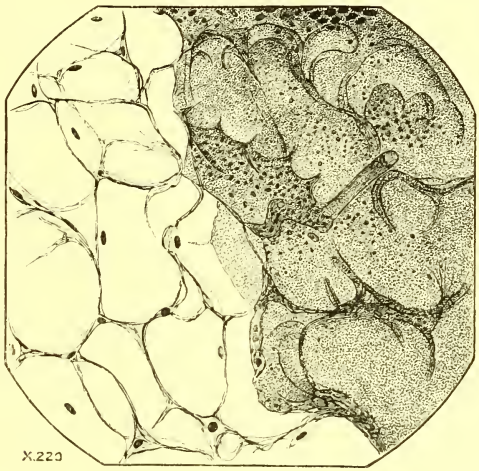


FIG. 4.—*Fat Necrosis.* The abrupt transition, from the healthy cells on the left to the necrosed cells on the right, is well marked. The contents of the affected cells are finely granular. (From a specimen by Dr. Rolleston.)

cells. Fat necrosis is most frequently encountered in the subperitoneal fat, but is occasionally met with elsewhere.

Pathology.—Four distinct explanations of this change in the fat have been offered. According to Balser and Zenker it is a primary necrosis of fat, following its excessive growth, and occurring therefore in fat people. Balser also noted its association with hæmorrhage in the neighbourhood of the pancreas and surrounding parts. Langerhans attributes it to the destructive action of steapsin absorbed from the intestine. Fitz, recognising the frequency with which it is associated with pancreatitis, considers that it is due to the spread of inflammation from the pancreas itself. Rolleston* raises objections to all these views, and draws attention to the occurrence of the change in conditions due to severe disturbance of the abdominal sympathetic. He points out that in acute lesions of the pancreas the solar plexus

* Trans. Path. Soc. of Lond., 1893.

is likely to be involved, and suggests that "fat necrosis" should be regarded as a disturbance due to some affection of the abdominal sympathetic. In this way, its ordinary *distribution*, its *associations* with inflammatory conditions near the head of the pancreas, and the *symptoms*, resembling those of acute intestinal obstruction, which frequently accompany it, are all, to a certain extent, capable of explanation.

Post-Mortem Changes.

The changes which always occur in tissues after death must now be considered more particularly. First, with regard to the blood: this fluid undergoes the earliest and most rapid change. The hæmoglobin escapes from the red corpuscles, partly by exudation, and partly by the destruction of the corpuscles themselves, and, dissolved in the liquor sanguinis, permeates the surrounding tissues. The corpuscles are ultimately completely annihilated, nothing remaining but a few minute granules. The staining of the tissues with hæmoglobin is commonly known as **post-mortem staining**, and the appearances it presents are very characteristic. The lining membrane of the heart and blood-vessels, being in immediate contact with the blood after death, are the parts principally affected. The dissolved hæmoglobin also soaks through the walls of the veins, thus giving rise, on the surface of the skin, to red lines which mark the position of the vessels lying beneath. The staining is of an uniform pinkish-red colour, thus differing from the punctiform and stratiform redness of hyperæmia, from which it must be carefully distinguished. The amount of staining is in proportion to the rapidity with which decomposition has taken place, and to the amount of blood contained in the part at the time of death. Marked staining of the endocardium and great vessels occurs very rapidly after death from septicæmia.

Post-mortem discoloration must be distinguished from post-mortem staining. It is a purplish colour seen in dependent parts which are not pressed upon, and is due to the gravitation of fluid blood into the vessels of these parts. It disappears if the body be turned over.

In muscle the arrest of nutrition is accompanied by a state of rigidity known as **Rigor Mortis**. This is a peculiar condition of the muscles observed in almost all bodies after death, in which they become firm and somewhat shortened, as though in a state of permanent contraction. It comes on as soon as the muscles have lost their

irritability—*i.e.*, their capability of responding to artificial stimulation; in other words, as soon as the nutritive processes have completely ceased. The time of its appearance will therefore depend upon the state of nutrition of the muscles at the time of death; the more healthy and vigorous this is the longer it is before the nutritive processes completely cease, and consequently the longer it is before the rigor mortis supervenes. The length of its duration and its intensity are in direct proportion to the lateness of its appearance. In people, for example, who are in perfect health and die suddenly, as from accident, the rigor mortis does not usually come on until from ten to twenty-four hours after death; it is very marked, and often lasts two or three days. In those, on the other hand, who die from some exhausting disease, as from chronic phthisis, or the adynamic fevers, in which the nutrition of the muscles becomes much impaired, the rigor mortis appears very soon, sometimes as early as ten minutes after death; it is very slight, and may pass off in less than an hour. It has been said that in cases of death from lightning, and from some of the severer forms of the adynamic fevers, the rigor mortis is entirely absent. It is doubtful, however, if this is the case, as the rigor mortis has probably escaped observation, owing to its early supervention and rapid disappearance. As soon as the rigor mortis has passed off, decomposition of the muscular tissue commences.

With regard to the nature of the change, Kühne and others have shown that it is really owing to the coagulation of the albuminous substance of the muscle—myosin. The myosin, fluid during life, coagulates when nutrition has ceased, the coagulation being attended by the liberation of a free acid. Thus are produced the firmness, hardness, and opacity of the muscle together characteristic of rigor mortis. These disappear as soon as decomposition commences. The transverse striation of the fibres then becomes indistinct, and gives place to irregular rows of granules and fat-molecules. In the meantime the muscle softens, its sarcolemma disappears, and ultimately nothing remains but a soft structureless débris. This change is not confined to muscle; in the cells of other tissues a similar coagulation of the protoplasm takes place on the cessation of the nutritive processes.

Respecting the *post-mortem* changes in other tissues—protoplasm generally not only coagulates, but tends to become finely granular after death. It sometimes increases in bulk so that the cells look swollen; and in nucleated cells the nucleus often shrinks or entirely

disappears. The cells ultimately break up into molecules of various sizes. In adipose tissue, the cells diminish in size, owing to the escape of the fluid fat, which diffuses itself throughout the surrounding structures. The fibres of connective-tissue swell up, become opaque, and ultimately liquefy. In nerve-fibres, the white substance of Schwann coagulates and collects into small drops within the neurilemma. Cartilage, bone and hair resist the putrefactive process longer than any of the other tissues, and are the least altered by it.

CHAPTER II.

NUTRITION IMPAIRED.

It has been shown in the preceding chapter that the complete and permanent arrest of nutrition in a part causes death, that is, cessation of function. We have now to consider those morbid processes in which *nutrition* is more or less *impaired*, and in which, therefore, pro portionate *diminution of* functional activity will be the characteristic consequence. Nutrition may be impaired in two ways: in *quantity*, so that waste comes to be in excess of assimilation, or in *quality*, either the food or the metabolism of the cell being abnormal. Excess of waste over assimilation leads simply to **atrophy**, or simple diminution in the size of a part or of the whole body, whence results impairment of its functional powers. On the other hand, alteration in the chemistry of the cell, or in the quality of the food supplied to it, *may* lead to **degeneration** of the cell-contents: some abnormal substance appears in the tissues, formed by metamorphosis of the cell-protoplasm, or deposited in the cells by the blood and not consumed. This, again, causes more or less impairment of the functions of the degenerate tissue elements. Both atrophy and degeneration must therefore be regarded as stages towards death; and, in both cases, the impairment of nutrition not uncommonly becomes so extreme that it amounts at certain spots to absolute arrest. Death of the most affected cells consequently ensues.

Several abnormal substances may appear in the tissues as results of their degeneration, and according as these substances are believed to be derived from the cell-protoplasm itself or to be merely deposits from the blood, the degenerative processes are divided into two

groups: the **metamorphoses** or **degenerations** proper, and the **infiltrations**. They differ essentially. In the **metamorphoses** the cell-protoplasm is gradually transformed into a new material. This process is often continued until complete destruction of the histological elements has taken place, and all trace of the original structure is lost. In the earlier stages of the process function is impaired: in the later it may be completely arrested. In the **infiltrations** the new material is not derived from the cell-protoplasm, but is deposited from the blood; there is an infiltration of a new substance. This is rarely followed by destruction of any of the histological elements, hence the structure of the tissue is much less altered than in the metamorphoses, and function is usually much less interfered with.

The **metamorphoses** are: fatty, mucoid, colloid, and probably albuminoid. The **infiltrations** are: fatty, calcareous, and pigmentary.

Atrophy.

Atrophy must be carefully distinguished from arrested development. It is a *decrease* in the amount of a tissue, owing to diminution either in *size* (**simple atrophy**) or *number* (**numerical atrophy**) of the histological elements of which it is composed. It is attended by loss of weight and impairment of function. The two varieties, simple and numerical, are often associated, the latter being an advanced stage of the former.

Atrophy may be **general**, affecting to a greater or less extent all the organs and tissues of the body, or it may be **local** and therefore limited to particular parts. In general wasting the stress falls at first upon the subcutaneous adipose tissue, then upon fat in other situations, as around viscera and in the omentum, then upon the muscles and glandular organs, and lastly and least upon the osseous and nervous structures.

MICROSCOPIC APPEARANCES.—Diminution in size is the most common condition met with in atrophy, and may affect all tissues, as is well shown in ordinary emaciation. Thus adipose tissue is merely common connective-tissue, many cells of which are distended with fat. When a person emaciates, the fat is gradually removed from the cells, which diminish in size, and the fat which once filled them completely may be reduced to a few isolated drops; it is usually partially replaced by serous fluid. The cell-wall and nucleus often

become distinctly visible (Fig. 5), and multiplication of the nucleus is not infrequently observed (*atrophic proliferation*). This example, though usually given, is not a good one, inasmuch as the diminution in size of the cells is due to the absorption of a substance with which they have been *infiltrated*, and which is not essential to their well-being, whilst the protoplasm, at first at all events, is not affected. The cells of all glands may undergo true atrophy; they become smaller, being often finely granular from the presence of molecular fat. Shrinking of the whole organ results. Muscular tissue also may

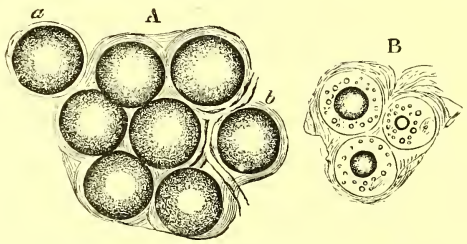


FIG. 5.—*Adipose Tissue.* A. Normal. B. Atrophic, from a case of phthisis. *a*. A single fat-cell, with cell-wall, nucleus, and drop of fat. × 300. (Virchow.)

atrophy by simple diminution in the size of its primitive fasciculi; and here, as in adipose tissue, atrophic proliferation of the muscle-nuclei seems to be common.

Unless their *vital activity* is exhausted the shrunken cells are capable of recovery; all that is necessary for their restitution is diminution of waste or increase of assimilation, according as one or other is faulty.

Numerical atrophy is often an advanced stage of *simple atrophy.* The elements not only diminish in size, but some actually perish, as is well seen in advanced atrophies of muscle; then restitution is possible only by the production of new elements, whereas in *simple atrophy* repair can be effected without new formation. In certain tissues—as the spleen, lymphatic glands and skin—in which growth occurs by addition of new elements, and not by enlargement of pre-existing cells, atrophy is probably always due mainly to numerical loss.

Although atrophy in its strict signification consists simply in a diminution in size or in number of the component elements of a tissue, it *is rarely a perfectly simple process,* but is usually associated with more or less *fatty degeneration.* This indicates fault in the chemical processes of the cells. Probably, when the nutrition of a part is so much inter-

fered with as to cause it to atrophy, those portions of its cells, which should be combined with oxygen and rendered soluble, remain; fatty degeneration is the natural fate of protoplasm under such conditions. It is possible, too, that an atrophying tissue would not store sufficient oxygen for its use. It will be seen subsequently that fatty degeneration arises from causes similar to those which produce atrophy itself.

PHYSICAL CHARACTERS.—The naked-eye recognition of atrophy is often difficult. Atrophied organs are *usually* diminished in weight and size. They also contain less blood, and are drier, paler, firmer, and more fibrous-looking than in health. The great criterion is *diminution in weight and size* of an organ; but these vary considerably in health—especially with the weight and size of the whole body; moreover, they may be small from incomplete development. Again, accumulation of blood and other fluids in an organ may bring its weight and size up to or above the average, although its essential tissue is considerably diminished in amount. The same fallacy may arise from overgrowth of the fibrous stroma of an organ.

All the tissues of which an organ consists may waste simultaneously, but the term "atrophy" implies, primarily and chiefly, wasting of its characteristic cells, as opposed to the stroma. The vessels and nerves of course share in the wasting process. The fibrous constituents are the last to atrophy; and this fact, together with the diminished blood-supply accounts for the pallor, dryness, toughness, and fibrous appearance above-mentioned as usual in atrophied organs. Not uncommonly, as the higher cells shrink and disappear, the connective tissue of the organ *increases*—as in the secondary "scleroses" of the spinal cord—and it may become the seat of fat-infiltration, as in pseudo-hypertrophic muscular paralysis. This tendency to take advantage of the obvious weakness of a contiguous tissue is perhaps to be explained by Cohnheim's theory of the "physiological resistance" offered by one tissue against invasion of its territory by another (see "Tumours"). More probably, however, the overgrowth of connective-tissue in such cases is due to a general attempt at repair which only results in the increased growth of the least specialised and most easily regenerated tissue.

ÆTIOLOGY.—The occurrence of atrophy is sure evidence that the nutritive exchange in the atrophied part is disturbed so that *waste exceeds assimilation.* This is *the immediate cause of all atrophies. Assimilation* may be deficient because of *insufficient supply* of food, or because

of *inability* on the part of the tissues *to use* the food supplied. The circumstances which excite excessive waste in individual cells are but little understood. It is convenient to speak of *general* atrophy as distinct from *local*.

General Atrophy may be caused by :

1. **Deficient Supply of Nutritive Material.**—Whatever interferes with the supply of nutritive material to the tissues will be followed by their atrophy. Thus the following conditions may all be causes of general atrophy : deficient supply of food ; obstruction to the passage of food into the stomach or intestines, as in stricture of the œsophagus or pylorus ; the mal-assimilation which results from the various conditions giving rise to dyspepsia ; interference with the absorption of the chyle, from obstruction of the thoracic duct, or from disease of the mesenteric glands constituting the so-called "tabes mesenterica."

2. **Excessive Waste.**—All conditions attended by the loss of large quantities of nutritive material may also be causes of general atrophy. Among these are : continuous hæmorrhages ; profuse and long-continued suppuration from chronic bone-disease or empyema ; diarrhœa ; and the excretion of large quantities of albumin in Bright's disease or of sugar in diabetes mellitus. The waste from increased tissue-change accompanying acute febrile diseases must also be included under this head.

3. **Impaired Vital Activity.**—This constitutes an important element in the production of the atrophy of old age—**senile atrophy**. As life advances, the ability of the elements to perform those chemical processes which are necessary for the preparation and assimilation of the tissue-food diminishes more rapidly than the ability to perform those which are concerned with the production of the waste products. Hence, these elements gradually atrophy ; and ultimately all manifestations of their vitality may cease.

Although general atrophy may occasionally be referred to one of the foregoing causes, it is usually due to the combined influence of two or more of them. The atrophy associated with pulmonary phthisis, for example, results partly from *loss of nutritive material* in profuse expectoration and diarrhœa, partly from *deficient supply* consequent upon imperfect oxidation of the blood and upon interference with assimilation which is so often caused by structural changes in the stomach and intestines, and partly from the *increased tissue-waste* of fever. In senile atrophy again, in addition to the general diminution of nutritive activity, there is frequently some condition of the digestive organs,

which interferes with assimilation: this materially aids in producing the ultimate result. Increased tissue-waste, loss of appetite, and interference with assimilation all help to produce the atrophy which accompanies fever.

LOCAL ATROPHY.—In local atrophy, it is often very difficult to discover which factor in the nutritive exchange is at fault.

1. **Deficient Supply of Nutritive Material.**—The effect of diminishing the blood-supply to a part will vary, according to the degree of the diminution, from slight atrophy to absolute necrosis.

Diminished supply of arterial blood is a common cause of atrophy (*passive*), and may be brought about in various ways. (1) *By obstruction of the supplying vessels before they enter a part.* Thus pressure of an abdominal aneurysm on the spermatic artery may cause atrophy of the testis; and fracture of a long bone, above the point where its nutrient artery enters, may result in wasting of the upper fragment. (2) *By uniform and continuous pressure* which does not compress the veins disproportionately. Thus atrophy, even of bones, results from pressure of aneurysms and tumours; deep fissures are formed in solid organs from pressure of band-like adhesions; atrophy of the kidneys will follow obstruction in the urinary passages; and, rarely, wasting of a testis may be due to pressure of old hæmatoceles or hydroceles. Pressure may also arise within the capsule of an organ by the appearance of some new growth or inflammatory effusion—especially that leading to the formation of young, strongly contractile cicatricial tissue. The effect of this is seen in cirrhosis of the liver, and, according to some pathologists, in granular contracted kidney. In all "pressure atrophies" the constant pressure also acts directly on the cells of the part and thus impairs their powers. (3) *Mechanical congestion* in the same way sometimes leads to atrophy. The circulation is impeded, and the blood is not returned normally by the veins. Hence there is deficient arterial supply, and atrophy results. This is seen, for example, in the mechanically congested liver of heart disease.

2. **Diminished Functional Activity.**—Atrophy always causes diminished functional activity; but sometimes diminished *functional activity* seems to be itself the cause of atrophy. In these cases the immediate cause is either *deficient supply of food* or *impaired vital energy.*

Diminished functional activity of a part implies that the chemical

processes in its cells are less active than normal; such cells require less food. How the needs of each tissue are made known to the blood-forming organs is not understood; but the supply is, as a rule, speedily adapted to any variation in the demand. Consequently, tissues will, soon after they have ceased to perform their functions, receive only sufficient material for those chemical processes which still go on in them. This is insufficient to maintain the mass of protoplasm required to do the full work of the tissue; so some of it atrophies.

After birth, those parts which are no longer required in the altered circulation gradually atrophy. The umbilical arteries and vein become thrombosed up to their first branches, and shrink to a fibrous cord as the clots organise—just like any other vessel cut across or tied. But this does not explain the closure of the ductus venosus or ductus arteriosus, in which the conditions are not favourable to thrombosis. Obliteration of these vessels can at present be spoken of simply as a developmental fact, comparable to closure of the foramen ovale. The Wolffian body disappears as the kidneys develop, and the thymus wastes in the second year. These, perhaps, are examples of atrophy of organs following the development of others better fitted to do the work—illustrating, as it were, the converse of the law that when an organ atrophies or is removed, correlated organs hypertrophy and take on its function. (See "Hypertrophy.")

Muscles atrophy when they are rendered inactive by chronic disease of joints, by splints, or by paralysis from disease or injury of the nervous system *above* the anterior cornual cells with which they are connected—*i.e.*, by an "upper segment" lesion. When the muscles of a part waste, all its other tissues—nerves, vessels, bones, &c.—suffer ultimately from impaired blood-supply. Thus, in part at least, we may explain wasting of the bone in a stump or limb long kept at rest; the absence of that intermittent pressure, which it is the function of bones to bear, is probably a secondary cause: at all events, increased strain causes hypertrophy of a bone. After removal of the distal part of a limb, the main artery and branches supplying it become smaller and thinner. The rectum dwindles after colotomy to a scarcely pervious cord: in this case the passage of fæces over the mucous membrane no doubt acts as a stimulant to its vessels, as well as an excitant of muscular action, and, as, after colotomy, the rectum is never distended, its tissues adapt themselves to the empty condition. Atrophy of the stump of the optic nerve follows removal of the corresponding eyeball.

The female generative organs atrophy at from forty-five to fifty years of age, the male somewhat later; the spleen and whole lymphatic system waste after middle life: probably in these cases the vital energy of the cells of the parts concerned is exhausted about the times mentioned, and diminished function is the result—not the cause. Thus these are really examples of "senile decay."

Trophoneuroses.—When a muscle is *cut off from* its connection with the *cells in the anterior cornu,* or when these cells are destroyed or seriously injured, fatty degeneration of the muscle, a more rapid process than simple atrophy, sets in. In the case of atrophy, those changes which nervous stimuli alone can excite (p. 7) probably go on; but in the former they are completely arrested. Examples of this atrophy are afforded by the acute bulbar and spinal paralyses of adults, infantile paralysis, some cases of progressive muscular atrophy, neuritis from any cause, and rupture, contusion, or section of a nerve. Salivary glands waste on section of their nerves. Nerves cut off from their ganglion cells (of which they are long processes) also degenerate rapidly and waste. In all these cases the interstitial connective-tissue increases, and often becomes loaded with fat as the higher tissue disappears.

3. **Excessive Functional Activity.**—This may, quite exceptionally, be a cause of atrophy—*e.g.,* of the testis, and possibly of the kidney. This will be further discussed in the section on Chronic Interstitial Nephritis.

Atrophy of Bone.

As in other tissues, atrophy of bone is usually accompanied by more or less fatty degeneration. *Old age, disuse,* and *constant pressure* are its most frequent causes.

When due to *old age,* there is diminution in weight but no change in size. The loss of weight is the result of the gradual conversion of the compact tissue into one closely resembling the cancellous. The spaces become larger and their bony walls thinner; the consequent brittleness of the bone is therefore a marked feature. This form, known as **eccentric atrophy,** occurs with other senile changes, and generally affects all bones, but is specially marked in the neck of the femur, rendering it liable to fracture from trivial injuries.

Atrophy from *disuse* or from *constant pressure* is accompanied by diminution in size as well as in weight. The bone beneath the periosteum is gradually absorbed, and the medullary canal shrinks

proportionately. This variety is known as **concentric atrophy**, but the changes characteristic of the *eccentric* form are often present as well. It is a local alteration, and is met with especially in the long bones, in cases of long-standing ankylosis, dislocation, or paralysis. The effect of constant pressure in the production of atrophy is well shown in the enlargement of clefts and perforations of the hard palate which often results from the insertion of plugs. These interfere with the blood-supply and thus cause atrophy.

Atrophy of bone must not be confounded with *arrested development*. The latter is commonly met with in the later stages of infantile paralysis. A very similar result may be produced by anything which causes premature ossification of an epiphysis, such as rickets, inflammation or injury. These are the common causes of stunted limbs; and microcephaly may be due to premature ossification of the cartilage between the basi-sphenoid and the basi-occipital. .

Pulmonary Vesicular Emphysema.

This appears to be a proper place to describe the changes in the lungs in emphysema, as the chief of them is atrophy of the inter-alveolar septa.

Emphysema consists essentially in a *permanent* enlargement of the infundibula and air-cells due to atrophy of the intervening septa; it should be distinguished from the acute over-distension often seen, especially in children, after death from bronchitis or hooping cough. The condition of the lungs met with in these diseases is sometimes called "acute emphysema."

VARIETIES.—Two varieties are described: (1) Hypertrophous or "large-lunged" emphysema—by far the most important, and always indicated when the term "emphysema" alone is used; (2) Atrophous, small-lunged, or senile emphysema.

1. In **Hypertrophous Emphysema** the lungs are enlarged, sometimes so much that they actually cross in the mid-line in front, obliterate the superficial cardiac dulness, project markedly into the neck, and push down the diaphragm. Owing to the loss of their elasticity the lungs collapse but slightly when the chest is opened, and their usually sharp edges (in front and round the base) are pale, thick, round, and more or less irregular from the protrusion of soft, pale, rounded swellings: similar swellings frequently project towards the

diaphragm; the tongue-like piece of the left lung below the notch is often extremely swollen, and the lungs may bear distinct grooves corresponding to the ribs. Everywhere, in advanced cases, the air-cells are seen through the visceral pleura with abnormal distinctness; but the apices and sharp edges are first and chiefly affected, and spaces of considerable size are here met with. Abnormal pigmentation is



FIG. 6.—*Emphysema of the Lung* (from a case of chronic bronchitis). A portion of the rounded anterior edge of the lung. The varied size of the cavities formed by distension of the alveoli and atrophy of the partitions is well shown. (From a specimen by Dr. Arkle.)

usual. The lungs feel much like a down-pillow, they "pit" easily, and crepitate but little. On section the emphysematous parts are pale, dry and bloodless; and when large spaces are present in the part cut, the collapse of the affected areas is very marked.

Microscopic investigation shows: that the dilatation commences in the infundibula, and extends thence into the alveoli opening into it; that the inter-alveolar septa atrophy and ultimately become perforated, their elastic fibres yielding and then disappearing; that the stretched capillaries become thrombosed, and then likewise vanish. The apertures in the inter-alveolar septa enlarge; and, later, others

form between the infundibula, and thus are developed irregular cavities, which are sometimes as large as a filbert. The largest are situate in the pale, rounded, bleb-like swellings. Fatty degeneration of the alveolar epithelium is commonly present, and is probably secondary to vascular disturbance.

The communications between the pulmonary and bronchial vessels become dilated. The connective-tissue round the smaller bronchi may be increased as the result of bronchitis.

Hypertrophy or dilatation of the right ventricle (p. 100) frequently results from the obstruction to the pulmonary circulation, any marked dilatation being accompanied by the venous congestion of cardiac failure. The thorax becomes barrel-shaped—almost fixed in a position of full inspiration.

2. **Atrophous Emphysema** occurs usually in thin old people who seem to be undergoing general atrophy. The lungs during life may leave the heart unduly exposed; when the thorax is opened they collapse excessively, falling together "like an inflated bag of wet paper" (Jenner). They are excessively pigmented, and their apices and borders, even after collapse has occurred, usually show appearances like those in the large-lunged variety, and are due to similar naked-eye and microscopic changes. In this form, apparently, the elastic tissue is not so generally affected as in the large-lunged variety.

ÆTIOLOGY.—All conditions which increase, either *absolutely* or *relatively*, the pressure on the inside of the air-vesicles, or which weaken their walls, may act as causes of emphysema.

(1) *Intra-alveolar pressure increased absolutely.*—Increased pressure in the air-cells may be due to violent expiratory efforts with closed glottis, as in coughing; to violent muscular efforts while the glottis is closed and the thorax distended; and to the blowing of wind instruments. Those parts of the lungs which are least supported—the apices and edges—will be most affected. This is the *expiratory theory* of Jenner. Emphysema due to causes such as these is often called *primary*.

(2) *Intra-alveolar pressure increased relatively.*—When, by reason of collapse, compression, or consolidation, the entrance of air into, and the consequent expansion of, any part of a lung are interfered with, inspiration will tend to produce a vacuum in the immediate neighbourhood of this portion with greater force than in other parts, and the air-cells in this particular neighbourhood will therefore tend to become

more distended than those in other parts. Similarly, when from the same cause a whole lung fails to expand, its fellow stretches over towards it, and even the mediastinal contents may be displaced in the same direction. This form of emphysema is termed *vicarious, compensatory,* or *secondary,* and this explanation of its causation is known as the *inspiratory* theory.

(3) *Weakening of the alveolar walls.*—This weakening may be due to (*a*) the atrophy and loss of elasticity which accompanies old age—the most important element in the causation of atrophous emphysema; (*b*) atrophy following the stretching, narrowing, and obliteration of the blood-vessels, which in its turn is a result of over-distension of the air-cells from any of the causes before mentioned; and (*c*) inherited weakness (emphysema may run in families), or weakness due to some interference with their nutrition, from the mode of living or other causes.

CHAPTER III.

FATTY DEGENERATION.

The term **Fatty Degeneration** is here used to include all cases of abnormal accumulation of fat in the tissues; but it is frequently employed as synonymous with "fatty metamorphosis," and as opposed to "fatty infiltration."

The abnormal accumulation of fat in the tissues may result from either infiltration or metamorphosis (p. 29)—two essentially different processes as regards causes, nature and effects. Examples of both occur in health (pp. 45, 48).

According to Cohnheim, all fat found in the body has the same chemical composition—being a mixture of tripalmitin, triolein, and tristearin. It has since been shown* that if dogs are fed on colza-oil, linseed-oil, or mutton-fat, the melting point of the deposited fat will vary with that of the form in which it was given, and that, in the case of the colza-oil diet, the tissues will contain erucic acid, which under ordinary conditions is absent.

* Lebedeff and Munk, quoted by Bunge.

FATTY INFILTRATION.

In fatty infiltration, fat brought by the blood is taken up and deposited in the substance of certain cells—viz., those of the *connective-tissue* of certain parts (especially subcutaneous and subserous): those of the *medulla* of limb-bones; and to a less extent those of the *liver*, which thus serve, physiologically, as reservoirs of fat. It is impossible to draw any line between normal and pathological fatty infiltration so long as the process is confined to those cell-groups which are physiologically liable to this infiltration. Thus the subcutaneous fat and the fat normally present along the coronary vessels in middle-aged adults varies much in amount consistently with perfect health. But when the fat spreads widely over the surface of the heart it is clearly abnormal; and the evidence of disease is still stronger when the fat appears between the muscular fibres in cells which, normally, contain none. The tendency to morbid fatty infiltration may be **general** (*obesity*) or **local.**

CAUSES.—It may be stated generally that, whenever oxidisable material is present in the blood in excess of the amount required for the supply of force and maintenance of heat of the body, there is a tendency to the deposit (storage) of fat, first in regions in which it is normally present, and later in parts which usually contain none. For this, fat itself need not be present in excess in the food; the presence of carbohydrates in quantity sufficient to satisfy the wants of the organism will protect fat from oxidation. But it would seem that there are factors in the process of fattening other than the relation of **food supply** to **oxidation**, for nothing is more certain than that a tendency to obesity or to leanness runs in families, and it is notorious that some very stout people are small eaters and active, whilst many thin subjects are just the reverse. Cohnheim has, it is true, advanced the hypothesis that, in the former, oxidation is naturally slow and imperfect, but we know of no experimental facts in support of the view.

With regard to the sources of fat deposited in the body—the food-stuffs whence it is derived—many views are still held.

(1) It appears possible, from the facts stated on the preceding page, that some **fat** may be absorbed and deposited, without change, in the tissues, even when the food contains fat dissimilar in composition to that generally met with in the human body. On other occasions

if any fat of the food is stored in the body it must somewhere undergo the change (usually the loss of some hydrogen) necessary to assimilate it to human fat. It is generally held that, under ordinary circumstances, the cells will not take up from the blood fats which are not normal in them. The term "infiltration," which implies passiveness on the part of the cell, is therefore probably incorrect in these instances.

(2) It is generally believed that fat is not formed directly from **carbohydrates**, but that these take the place of the material

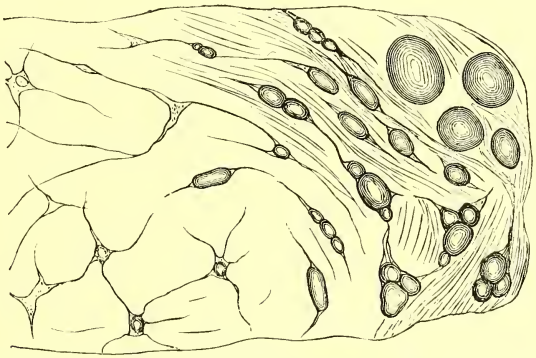


FIG. 7.—*Fatty Infiltration of Connective Tissue.* Showing the accumulation of fat within the cells. × 300 (Rindfleisch).

from which fat can be formed; there are, however, many facts in favour of the opposite view. Thus bees, while living on carbohydrates, continue to produce wax. In the case of pigs it has also been shown* that, under certain conditions, the deposit of fat is due to the carbohydrates in the food. Nothing is known concerning the nature of the change.

(3) It is thought that the chief source of fat deposited in the tissues is the **proteids** of the food. These are said to be absorbed and split into a nitrogenous and a non-nitrogenous molecule, from the latter of which fat is formed, and stored if not required.

It would appear, therefore, that **excess of the diet** over the wants of the body, particularly if the excess be in hydrocarbons or carbohydrates, is one great cause of fattening.

With regard to the second great cause—**diminished oxidation**—

* Tschervinsky and others, quoted by Bunge.

this may result, from sedentary and luxurious habits, ease of mind and body, high external temperature, destruction of much lung-tissue by chronic disease, or reduction of the oxygen-carrying power of the blood owing to diminution of red corpuscles or of their hæmoglobin. The fat contained in a normal diet may, under such circumstances, be incompletely oxidised. Locally, oxidation may be diminished by slow circulation or by the circulation of deoxidised blood through a part—conditions which normally obtain in the liver and in parts thrown out of work—as in a muscle kept at rest. Excesses of fat may sometimes be present in the fluids around certain cells—*e.g.*, the liver cells after a meal containing much fat, and the connective-tissue cells and wandering cells near a focus of fatty degeneration.

Thus to prevent fatty infiltration the *diet* should be moderate, carbohydrates, and alcohol, being as far as possible excluded. Appropriate exercise and the drinking of large quantities of water will favour oxidation, and ensure the prompt removal of waste products.

APPEARANCES.—1. **Microscopic.**—Cells undergoing fatty infiltration are seen to contain droplets of oil—very small at first, but still distinct droplets. These run together, push the cell-nucleus aside and distend the cell until its original contents seem to have become a mere capsule to the fat (Fig. 8). As the fat is added to the previous cell-contents, the cell is enlarged in proportion to the amount of fat it contains.

2. **Naked Eye.**—A fattily infiltrated organ is consequently more or less swollen. Any sharp edges it may possess tend to become thick and rounded. It is more or less pale and yellowish on account of anæmia (from increased intracapsular pressure) and the presence of fat; it is doughy and inelastic, and both receives and retains an impression from the pressure of a finger; and it is softer than natural. But, except mechanically, the fat does not hinder the protoplasm of the organ from discharging its functions. Ultimately, however, pressure upon the cells proper may become so severe that they may fail to get sufficient nourishment; they will then undergo fatty *metamorphosis,* and atrophy. The knife used to cut a fatty organ becomes greasy, and may show distinct oil drops on the blade.

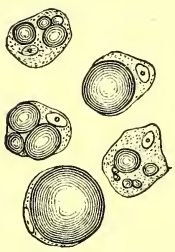


FIG. 8.—*Liver Cells in various stages of Fatty Infiltration.* × 300 (Rindfleisch).

SEATS.—The cells most commonly affected to a morbid extent are those physiologically liable to the process—viz., connective-tissue cells and liver cells: with regard to the former, it is to be noted that, normally, the cells of the interstitial connective tissue of working organs (muscles, nerves and glands) are not infiltrated, but may become so, especially if the activity of the organ, and the consequent afflux of arterial blood, are in any way arrested. In **obesity**—the commonest result of morbid fatty infiltration—the subcutaneous and subperitoneal connective tissue suffer earliest and most, the infiltration spreading later to the interstitial connective tissue of organs in which oxidation is still active. The process in connective tissue needs no description beyond that just given and illustrated by Figs. 7 and 9.

Fatty Infiltration of Muscle.

In muscle, fatty infiltration is common as a morbid process. The *cells in the connective tissue* which surrounds the fasciculi of the muscle become filled with fat; and this development of fat *between* the muscular fasciculi (Fig. 9) must not be confounded with degeneration of the fibres themselves. The interstitial fat varies in amount. In some cases single rows of fat-cells alternate with rows of muscular fasciculi; at other times the accumulation is less regular, more existing between some fibres than between others: in all but the most advanced cases, however, the muscular elements may, under the microscope, be discovered lying amongst the fat—even though, to the naked eye, the muscle appears to be entirely converted into fat. Ultimately the muscular fibres may undergo true fatty metamorphosis and atrophy until they completely disappear.

This condition is frequent in animals which have been fattened—the fat not only increasing in the usual situations, but also accumulating between the fasciculi of the muscles. It may also occur in muscles which from any cause have been incapacitated for some time, and in which, consequently, circulation and oxidation are reduced to a minimum. Thus it is found in long-standing paralyses from lesions of the brain or cord, and in muscles which have been rendered useless by ankylosis of a joint. In progressive muscular atrophy, and in chronic lead-poisoning the affected muscles exhibit this change, together with true fatty metamorphosis.

Fatty Infiltration of the Heart.—This is not infrequent in

general obesity, and after pericarditis followed by adhesion of the two contiguous surfaces. It must be carefully distinguished from the much graver condition of fatty degeneration. In health there is a varying amount of fat beneath the visceral pericardium, always most abundant around the vessels in the grooves between the auricles and ventricles. This may increase so as to cover the right ventricle, but the left is rarely, if ever, completely enveloped; at the same time the

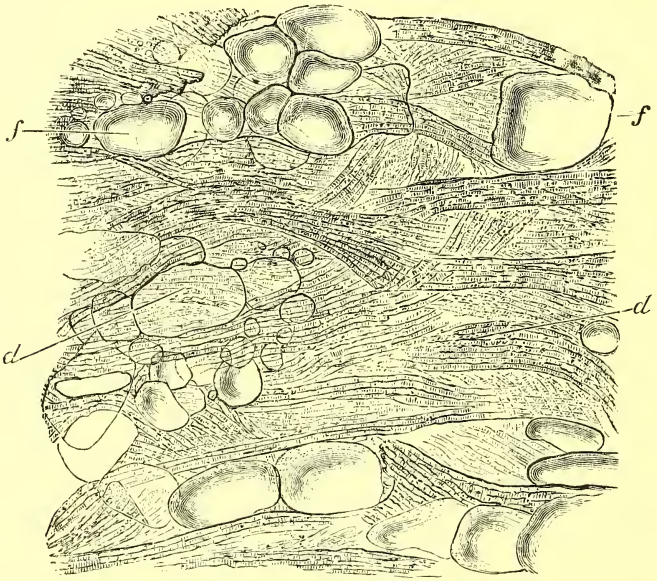


FIG. 9.—*Fatty Infiltration of Heart.* A section from the outer part of the left ventricle, showing growth of fat (*f*) *between* the muscular fibres. In some places fatty metamorphosis is commencing (*d*). × 200.

fat may push in along the vessels between the muscular fibres, so that, on the right side, to the naked eye, all appearance of muscular structure may be lost, the walls looking like a layer of fat, perhaps half an inch thick. In hearts less affected, striæ of fat, will be seen lying amongst the muscle. (Fig. 9). The fat is always most abundant near the surface, the muscular structure becoming more evident towards the endocardium: at the base of the ventricles thick villous processes may form.

The interstitial fat displaces and compresses the muscular fibres

between which it lies, and diminishes the blood-supply and contractile power of the muscle, perhaps ultimately causing true fatty metamorphosis of the muscle (p. 57). These two processes not uncommonly go hand in hand, but it is difficult to speak dogmatically as to which in any given case is primary: fatty infiltration is probably possible only as the functional activity of the heart (or any other) muscle sinks, and the continued action of the causes leading to this depression would ultimately cause degeneration of the fibres; the presence of interstitial fat must, however, tend in the same direction. Fatty degeneration and atrophy of muscular fibres, on the other hand, is very likely to be followed by interstitial infiltration.

Fatty Infiltration of the Liver.

CAUSES.—In the liver fatty infiltration is exceedingly frequent, constituting what is commonly known as the "fatty liver." This is owing—first, to the excess of non-nitrogenous oxidisable matter in the portal blood; secondly, to the deoxidised condition of the portal blood; and thirdly, to the low pressure and slowness of circulation in the portal vessels—conditions least favourable to oxidation, and most favourable to deposition of particles. An accumulation of fat in the liver thus occurs under two opposite conditions—one in which there is *general obesity*, and the fat accumulates in the liver in common with other parts; the other, in which there is *general emaciation*, and a consequent impairment of the oxygenating power of the blood. The liver in phthisis is an example of the second of these conditions, though in this case the defect in the oxygenating power of the blood is increased by the destruction of the lung tissue.

Physiological Infiltration.—The liver cells always contain a small quantity of fat, which is temporarily increased after the ingestion of fatty substances. Ingestion of food rich in fat is followed by a temporary excess of fat in the portal blood, and by the consequent deposition and temporary accumulation of part of this in the liver cells. This fat is first deposited in the *circumferential cells* of the lobules, that is, in those which are in immediate contact with the capillaries of the portal vein. From these it gradually passes to the central cells, whence it is ultimately conveyed again into the circulation. This process goes on until the excess of fat is removed from the blood, and the cells regain their former character. There is thus a

transitory accumulation of fat within the liver cells, but the vitality of the cells is not impaired thereby.

APPEARANCES.—1. **Microscopic.**—The morbidly fatty liver is one which constantly contains an abnormal quantity of fat, and here also, as the fat is usually deposited from the blood in the portal capillaries, the increase is first observable in the external zone of the



FIG. 10.—*Fatty Liver.* Showing accumulation of fat more especially in the cells of the external zone of the lobule. There is also some increase in the interlobular connective tissue (cirrhosis). V. Hepatic vein. I. Interlobular connective tissue. × 50.

hepatic lobules (Fig. 10). It accumulates here within the cells as minute globules which increase, coalesce, and form large drops of fat. These ultimately distend the cells, which become larger and more globular (Fig. 8). As the process advances, the infiltration spreads from the periphery towards the centre of the lobule, until its whole mass may be involved, and all its cells distended with fat. The vitality of the cells is not materially impaired by the infiltration, as is shown by the presence of bile in the stools and in the gall-bladder. In some exceptional cases the accumulation of fat is most marked around the intralobular veins. In these Virchow suggests that the fat is

becoming excreted, and that only the last cells retain a little of it. In extreme cases, such as sometimes occur in persons dying of cancer or phthisis, a section of the liver may look exactly like ordinary adipose tissue, being distinguishable from it only by a faint appearance of a radiating structure here and there, or an occasional section through the portal canal and its contained vessels.

2. **Naked Eye.**—The fatty liver is increased in size, in advanced stages to perhaps twice the normal. The surface is smooth, the edges are thickened and rounded, and the specific gravity is diminished so that detached portions may float in water, although the absolute weight of the whole organ may be increased. If the infiltration be slight, involving merely the portal zone of the lobules, the cut surface will present a mottled appearance, the external fatty zone being opaque yellowish-white, whilst the centre is unaltered or is hyperæmic and appears as a red spot (*fatty nutmeg-liver*). The more extensive the infiltration the larger is the pale zone, and ultimately, when the whole lobule is involved, there is left in the centre only a reddish-brown point—marking the position of the intralobular vein ; in many cases even this point is lost. Then the organ is of an almost uniform opaque yellowish-white colour, and the boundary between the individual lobules may be completely obscured. In exceptional cases the accumulation of fat is much more abundant in some portions of the liver than in others, so that on section yellowish points and streaks are seen scattered over its surface. The consistence of the organ is much diminished, it feels doughy, and pits on pressure with the finger, and the knife used to cut it becomes coated with oil. The pressure exercised by the infiltrated fat produces considerable anæmia of the organ, but the interference with the circulation is *never sufficient to cause ascites, hæmorrhage or other evidences of portal congestion.*

FATTY METAMORPHOSIS.

This differs from fatty infiltration, inasmuch as the fat is formed not from the fatty, saccharine, or nitrogenous principles of the food, but by metamorphosis of the protoplasm of the cells themselves. There is reason to believe that cell-protoplasm, as it becomes effete, takes up oxygen and splits into a nitrogenous molecule, which is the first stage in the formation of urea, and a non-nitrogenous molecule which

forms fat. To repair its loss, the living protoplasm, at the same time assimilates material it has prepared from the proteids of the food. In the process of healthy nutrition, destruction of small quantities of protoplasm and corresponding repair are constantly going on, and the products of the decomposition of effete albumin are still further oxidised, rendered soluble, and then at once removed. Consequently, we do not find in healthy cells fat granules bearing witness to the occurrence of the above described decomposition. When, however, a whole cell or many cells die and are protected from ferments, evidence of fatty metamorphosis of protoplasm is soon forthcoming. This we can watch in various physiological processes—*e.g.*, the formation of colostrum, sebum, and cerumen. In all of these the fatty degeneration, death, casting off and disintegration of superficial cells, and the constant production of new ones in the deeper layers, play a chief part. Evidence of the same process is seen in the fatty degeneration of the muscular fibres of the uterus undergoing involution. It was formerly supposed that the transformation of entire bodies, which have lain for many weeks or months in water or damp soil, into *adipocere*—(an ammonia and lime soap), was an illustration of the same process, but this change is now known to be due to organisms.

It is now universally recognised that the fat seen in the muscular fibres in fatty metamorphosis is the result of a change in the fibres themselves, and is not derived from without. The experiments of Voit and Bauer prove this. These experiments were made to determine the source of the fat in the acute fatty degeneration produced by poisoning with phosphorus. Dogs were starved for twelve days, so that all available fat, whether in the tissues or in the food, might be exhausted. At this period the daily excretion of nitrogen (urea) averaged eight grammes. Small doses of phosphorus were then given. The average daily excretion of nitrogen at once rose to twenty-four grammes, while the amount of oxygen taken up, and of carbon dioxide given off, were greatly diminished. The animals were then killed, and large quantities of fat were found throughout the body The increase in the excretion of urea showed that the destruction of proteids was also increased; and the presence of the large quantities of fat found after death made it highly probable that it had been formed as part of the general proteid destruction. In other words, the phosphorus produced very extensive and general fatty degeneration, and the *fat must have arisen from the protoplasm of the cells.* Voit concluded from these investigations—1st. That the transformation of cell-albumin

is independent of the supply of oxygen, but that if oxygen be deficient, the fat and other products of the transformation, being incompletely oxidised, accumulate in the cell. 2nd. That the presence of fat in the cells may thus be due to increased transformation of the albumin, or to diminished oxidation of the products of its decomposition. 3rd. That the fatty degeneration in poisoning by phosphorus is due both to an increased transformation of the albumin of the cells, and to diminished oxidation of the fat and other products of the transformation.

Stolnikow and Gaule have recently published experiments which seem to show, as Cohnheim suggested, that fat can be produced by the decomposition of *lecithin*, the phosphuretted fat of the nervous system, and a constituent of many other tissues. According to these observers, glycero-phosphoric acid, stearic acid, and cholin are formed in the process.

CAUSES.—A study of various examples of fatty metamorphosis renders it clear that the occurrence of this change indicates the decay of the protoplasm concerned; that the larger the proportion of the cell-albumin replaced by fat the nearer is the whole cell to death; and that the nearer the cell is to death the more impaired will be its power of taking up oxygen and combining it with effete materials. Consequently, we may give the cause of fatty metamorphosis as *grave depression of the vital activity* of a cell—leading to, (1) too rapid destruction of protoplasm, (2) lessened ability to repair losses, and, (3) impaired oxidising power. This depressed vitality is always the *proximate cause*, and is usually induced by (*a*) alteration in the quantity and quality of the food brought to the cell; or (*b*) by change in the physical condition of the cell; or (*c*) by the gradual but natural death of the cell—for there is a natural limit to the life of a single cell as there is to the life of the whole organism.

a. The effect of diminishing the blood-supply (*i.e.*, food and oxygen) to a part is seen in the fatty degeneration of the heart-walls which follows atheromatous changes in the coronary arteries, as well as in organs in which the lumen of the vessels is diminished by lardaceous or syphilitic changes. Working organs and tissues which have been long disused, and to which, consequently, the blood-supply is diminished, undergo fatty changes and atrophy until they become so small that the blood-supply is sufficient to maintain the nutritive equilibrium. Impaired circulation in a part—*e.g.*, mechanical congestion—has a similar effect. Fatty degeneration of the cells of cancers and other

rapidly growing tumours and of inflammatory exudations is often due to insufficient blood-supply; but the cells may be naturally short-lived, and in inflammation the cause of the process must have an injurious action upon the leucocytes as well as upon the fixed cells. These variations in the *quantity* of the blood-supply act *locally* (p. 59). Alterations in the *quality* of the blood-supply act *generally*, and all cells are thus liable to be affected. Thus, fatty metamorphosis of the most important organs may result from various forms of anæmia, from scurvy, and from the addition to the blood of a protoplasmic poison, like phosphorus, arsenic, or antimony. Poisoning by carbon monoxide has a similar effect, due to the power this gas possesses of combining with oxygen and thus preventing the oxygen from reaching the tissues. It is sometimes maintained that the presence of an excess of carbon dioxide is a more important factor in the production of fatty changes than any deficiency in the supply of oxygen.

b. The action of fever as a cause of fatty metamorphosis depends partly on the action of a high temperature on protoplasm; but the causes of the specific fevers and other circumstances probably give rise to blood-changes which act in the same direction. A high external temperature tends to diminish oxidation. (See "Fever.")

c. When the limit of life of a cell is approached, it undergoes fatty degeneration: thus we account for *senile* fatty metamorphosis of the cells of cartilage, cornea, bone and other parts. Under this heading may be included the fatty degeneration of nerves which follows interruption of their connection with their corresponding cells. Such degeneration seems to be the direct result of the loss of the normal physiological stimulus (Fig. 41, p. 108).

APPEARANCES.—1. **Microscopic.**—The process consists in the transformation of the protoplasm of cells into molecular fat, which appears as minute granules, first of all in the protoplasm and later on in the nucleus. The granules—characterised by their small size, sharp contour, strong refractive power, staining reaction (black with osmic acid), insolubility in acetic acid, and solubility in ether—gradually increase in number, till the whole of the protoplasm may be transformed; some of them may coalesce, and form distinct drops of fat. As the process advances the cells undergo an increase in size and become more globular in shape, the nucleus becomes involved, the cell-wall, when this exists, is destroyed, and the cell may thus be converted into a mass of fat-granules known as a granule-cell (Fig. 11).

Granule-cells may be of two kinds: (1) dead or dying cells converted into masses of cohering fat-granules, or (2), living leucocytes (*granule-carriers*) which have taken up fat-granules from a focus of degeneration—probably to convey them into the lymphatics and thus effect absorption. Connective-tissue and neuroglia-cells near foci of degeneration similarly become charged with fat-granules. Granule-cells are often called "inflammatory" corpuscles or "corpuscles of Gluge." Among typical granule-cells, formed by metamorphosis of epithelial cells or leucocytes, are the "colostrum" corpuscles of the first milk secreted; but later on the process becomes one of true secretion, and the resemblance ceases.



FIG. 11.—*Fatty Metamorphosis of Cells.* *a*. From a cancer. *b*. From the brain in chronic softening. The latter show the large "granule-cells," and also the manner in which these become disintegrated. × 200.

Ultimately fatty degeneration may affect connective-tissue fibres.

In old foci of fatty degeneration sheaf-like bundles of acicular crystals of margaric acid and rhombic crystals of cholesterin are found.

It is said that in fatty metamorphosis the percentage of fat in the tissue is but little increased, though this is disputed by Krehl;* apparently many of the granules are formed by the invisible fat which is normally bound up with protoplasm as it were in an "amalgam" (p. 2) (Birch-Hirschfeld).

2. **Naked Eye.**—In advanced stages fatty metamorphosis produces definite naked eye appearances. These are (1) slight or moderate swelling, which however is often replaced by more or less shrinking of the organ when absorption of the fat is going on, as in advanced acute atrophy of the liver; (2) admixture of an opaque yellow colour with the normal tint of the tissue, often in the form of patches, spots, or streaks, as extreme degrees of the change are usually reached only in limited areas; and (3) loss of elasticity with diminished consistence—the organ being flabby and friable, and its capsule wrinkling easily. Fat may be found upon the knife, and the normal distinctness of structure (upon section) is obscured.

* Krehl, *Deutsch. Archiv f. klin. Med.*, Bd. li.

The microscope is necessary in the **diagnosis** of the earlier stages of this metamorphosis. It reveals the granular and somewhat swollen state of the cells. The larger size, higher refractive power, insolubility in acetic acid, solubility in ether and blackening by osmic acid distinguish the fatty granules from the albuminous granules of "cloudy swelling," soon to be described. When possible, the distinction from fatty infiltration must also be made. Difficulty in this arises with regard to connective-tissue cells, liver cells, and intestinal epithelium —in which both infiltration or metamorphosis may occur; perhaps also the usual epithelium may contain infiltrated fat when this is being eliminated after severe contusions. The chief point of difference between the two processes is the size of the droplets, which are small in the metamorphosis but run readily together in the infiltration. This holds good as a rule, but infiltrated fat exists in small droplets at first and becomes finely divided before absorption, should this occur; on the other hand, large drops may form in fatty metamorphosis, and are characteristic in the liver in acute atrophy and phosphorus-poisoning, and in renal epithelium when the metamorphosis is at all advanced. Diagnosis may, therefore, occasionally be impossible. Evidence of destruction of cells is conclusive in favour of metamorphosis.

TERMINATIONS.—1. **Absorption.**—The fatty particles into which the cells have been transformed are, under favourable circumstances, readily absorbed. The degenerative process may cease and the fat be removed before the part has been dangerously involved. Such recovery probably often occurs, for example, in the kidneys and heart. Also when elements are completely degenerated the fatty débris is usually removed by absorption. This is seen in the fatty degeneration and absorption of inflammatory products, such as occurs in croupous pneumonia; in the degeneration and absorption of the cells of new growths—leading to central "cupping" or "umbilication" of nodules or to shrinking of the whole mass (atrophic scirrhus); and in the degeneration of small areas such as results from embolism, thrombosis, or hæmorrhage in the brain or other organ. As the result of such absorption we may have left a meshwork of vessels and connective-tissue whence the essential cells have disappeared, as in the later (red) stage of acute yellow atrophy; or we may have an ordinary scar, from the development of fibrous tissue; or, lastly, a cyst of clear fluid may remain. For absorption to occur, the tissues round the degenerated cells must be freely supplied with blood

2. **Caseation.**—In this mode of termination the fatty products are not absorbed, but are gradually converted into a yellowish friable material, which has been compared to soft cheese. It is generally said to result from disproportion between the degenerated mass and the vessels by which absorption might be effected—a disproportion which is, in the first instance, the principal cause of the degeneration. It is most frequent, therefore, in parts which contain but few vessels, or in which the vessels become obliterated by pressure from without or by thickening of their walls by endarteritis. Caseation is, consequently, most often met with in tubercular and gummatous masses, and in rapidly growing cancers and sarcomata.

Cheesy masses are constantly met with in the lymphatic glands, the brain, the bones, and especially in the lungs. Considerable confusion has arisen as to their nature and origin. Formerly all cheesy masses were regarded as essentially tubercular, and it is true that tubercular lesions have a greater tendency than any others to caseate fully, and to form *typical* cheesy collections (see "Tuberculosis"). But, as just stated, other formations may undergo a change which is practically indistinguishable; so caseation cannot be regarded as proving more than the occurrence of fatty degeneration. A caseous mass is tubercular only when it is due to the presence of the bacillus tuberculosis. Still it is doubtful if fatty degeneration of a gumma or of a rapidly growing tumour ever gives rise to a typical "caseous" mass such as we often find as the result of tubercular inflammation, and it has yet to be shown that caseation can occur apart from the action of some micro-organism.

The process consists in a gradual drying up of the degenerated elements; the fluids are absorbed, the cells—which are many of them incompletely degenerated—shrivel and atrophy, the fat undergoes partial saponification, cholesterin forms, and the tissue thus becomes converted into a soft, yellowish-white cheesy substance, composed of atrophied cells, fatty débris, and cholesterin crystals. This cheesy material may gradually dry up more and more, and ultimately become encapsuled by a layer of fibrous tissue, and even calcified. In other cases it may undergo a process of softening and liquefaction.

3. **Calcification.**—This is an advanced stage of the preceding process. It most frequently occurs when the caseous mass is completely shut off from the external air, as in lymphatic glands and bone, or when encapsuled in the lungs. The mass becomes infiltrated with

calcareous particles, and is thus converted into a calcareous concretion Single cells in a fatty focus may undergo this infiltration—*e.g.*, ganglion-cells in an area of cerebral softening.

4. **Softening.**—An inflammatory cell-exudation, usually of tubercular origin, may undergo fatty metamorphosis, and, as its cells break up into granules, sufficient fluid is often effused to form a thin puriform liquid, usually containing curd-like cheesy masses ; this looks like pus, but really consists of granules, fat drops, and perhaps cholesterin crystals suspended in fluid ("pathological milk"). This is the pathology of **chronic abscess** of tubercular origin. If not discharged, the fluid may be absorbed, leaving a caseous mass, which may calcify.

Sometimes, after long quiescence, caseous and even calcified masses appear to excite sufficient irritation to result in the formation of an abscess and in the discharge of the mass. The nature of the fresh irritant is unknown.

The **effect** of fatty metamorphosis is to impair or arrest function. Recovery is only possible in the earlier stages.

Fatty Degeneration of Blood-vessels.

Primary fatty degeneration of blood-vessels is in most cases a senile change ; it is an expression of that general impairment of vitality which exists in advanced life, and is usually associated with similar changes in other parts. There is, however, a variety limited to the lining membrane of the largest arteries : this is often met with in early life and in persons who are otherwise perfectly healthy.

Fatty Degeneration of Arteries.—This may be **primary** or **secondary** to atheroma or other inflammatory condition of the vessels, the fatty change being preceded by cell-infiltration of the sub-endothelial connective-tissue. (See "Atheroma.")

Primary fatty degeneration is not preceded by any disease of the parts affected by it. It may effect any or all of the coats of the artery, but is most commonly met with in the *intima*. The change usually commences in the endothelium and the sub-endothelial connective-tissue cells, small groups of cells becoming affected in various parts of the vessel ; and it may gradually extend from within outwards, the intercellular substance softening, until, in exceptional cases, the whole thickness of the intima is destroyed (Fig. 12).

In the earlier stages this condition is recognised by the existence of small, irregular, opaque, yellowish-white patches, projecting very slightly above the surface of the intima. These, which are so constantly met with on the lining membrane of the aorta, may at first be mistaken for atheroma. They are in most cases, however, readily distinguishable by their superficiality, and by the facility with which they can be stripped off from the subjacent layers, which present a natural appearance. In atheroma, on the other hand—which affects the deeper structures—if the superficial layer be removed, the opacity and thickening are seen to exist beneath it. In many cases the change is limited entirely to the innermost layers of the vessel. The more

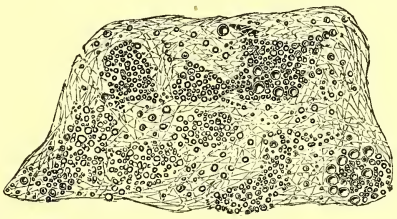


FIG. 12.—*Fatty Degeneration of the Internal Coat of the Aorta.* Small yellowish-white patches were scattered over the lining membrane of the vessel. A very thin layer was peeled off. The groups of fat molecules, and the distribution of fat in the intima are shown. × 200.

the subjacent tissues are involved, the greater is the irregularity in the shape of the patches, and the less readily can they be separated with the forceps.

The opaque patches occasionally break down. For this to happen the cells must become destroyed by the fatty change, and the intercellular substance softened. The granular débris thus formed is carried away by the circulation, leaving small, irregular, superficial erosions upon the lining membrane of the vessel. These erosions are not *ulcers* in the true sense of that term, not being the result of an inflammatory process. They resemble the superficial erosions so common upon the mucous membrane of the stomach.

Simple fatty degeneration may occur in any artery, but in the smaller ones it is especially liable to affect the external coat (Fig. 13), and in this situation its injurious influence is most marked. Here, by diminishing the elasticity and contractility of the vessels, it causes degenerative changes in the parts which they supply, and often leads

to rupture. This is exemplified by many cases of chronic cerebral softening and cerebral hæmorrhage, although in such instances atheromatous are generally associated with the simple fatty changes. In the larger arteries, as the aorta—where it is exceedingly common—it is of less importance : the more extensive process, atheroma, has a far more deleterious effect.

Fatty Degeneration of Capillaries.—Fatty changes are also found in the capillaries, especially in the nervous centres and the

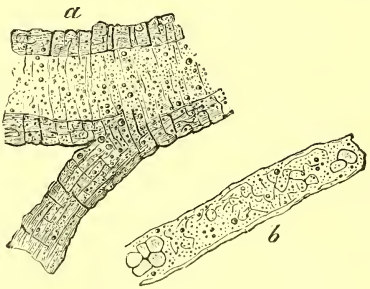


FIG. 13.—*Fatty Degeneration of small Vessels of Pia Mater.* From a case of chronic Bright's disease. *a*. A small artery, the coats of which are somewhat thickened. *b*. A capillary, in which are seen a few red blood-corpuscles. × 400.

kidneys—in Bright's disease (Fig. 13, *b*.). The process commences in the endothelial cells, and may involve considerable areas of the capillary wall, so that rupture is often the ultimate result. This is common in the smallest cerebral blood-vessels, where it is sometimes a cause of cerebral (capillary) hæmorrhage.

Fatty Degeneration of Muscle.

Both striated and non-striated muscle may be the seat of fatty degeneration. In both, the muscular fibre-cells are the seat of the change; they become filled with fat granules and are ultimately destroyed : the process thus differs essentially from **fatty infiltration** (p. 43).

Non-striated muscle.—Fatty metamorphosis is frequently met with in the middle coat of arteries undergoing fatty degeneration, and in the muscular fibres of a uterus in process of involution.

Striated muscle.—Both the voluntary muscles and the walls of

the heart show identical changes. The earliest stage of the affection is characterised by an indistinctness in the transverse markings of the fibres, which in many parts become studded with minute particles of fat (Fig. 14). These gradually increase in number and size, but almost always remain small, and are usually distributed somewhat irregularly within the sarcolemma. In some parts single or parallel rows of granules are found running along the length of the fibre; in others they are grouped around the nuclei, which they seem to lengthen, or arranged in transverse lines corresponding with the striæ of the muscle. The fibres become extremely friable, and are readily broken up into short fragments. As the process advances the transverse markings entirely disappear, and nothing but molecular fat and oil globules are seen within the sarcolemma. It has recently been affirmed that in some cases the striation is merely obscured by the fat droplets, and that these are in the early stages confined to the interfibrillary sarcoplasm. The sarcolemma itself may ultimately be destroyed, and nothing remain of the original fibre but the fatty débris into which its albuminous constituents have been converted. This is true "fatty degeneration" of muscle.

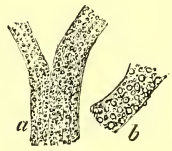


FIG. 14.—*Fatty Degeneration of Muscular Fibres of Heart.* *a*. Earlier stage. *b*. More advanced. × 400.

Fatty Degeneration of the Heart.

It is in the heart that fatty degeneration of muscle is most frequently met with, and here it assumes a most important aspect from the deleterious influence which it exercises upon the motor power of the organ. The degeneration may be *diffuse* or *circumscribed;* acute or chronic. The wider the extent of tissue that is affected, the less advanced, as a rule, is the degree of the degeneration. It is in those cases in which small tracts of tissue only are involved that the process is met with in its most advanced stage.

When the change is slight as in the **diffuse** form, the muscle is somewhat softer and more flabby than natural; it is more friable, and often breaks with a soft granular fracture; and its colour is rather paler and more opaque than that of healthy cardiac tissue. The microscope shows the muscular fibres to have lost to some extent their striation, and to contain granules of fat (Fig. 15, *a*).

The diffuse form of degeneration is caused by defects in the *quality*

or in the *amount* of the blood which is supplied to the heart walls. Thus it may be due to:—1. Diseases in which the *oxidation processes are reduced* to a minimum. This will be the case in diseases which are attended by marked anæmia, whether gradually or rapidly induced: such are anæmia from repeated or excessive bleeding, pernicious anæmia, advanced leukæmia, malignant and other cachexiæ. The accompanying drawing (Fig. 15) was taken from the case of a weakly young girl who was under my care suffering from slight valvular

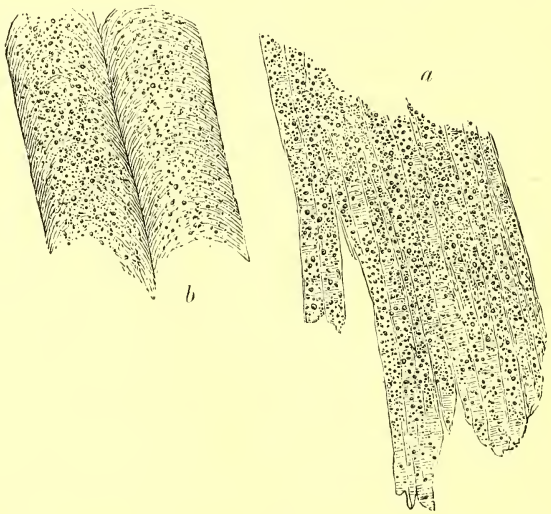


FIG. 15.—*Acute Fatty Degeneration of Heart and of other muscles.* *a*. Heart. *b*. Rectus abdominis. The whole of the heart-tissue was affected, and also the muscles in other parts of the body. × 400.

disease. She quickly succumbed with acute fatty degeneration of the heart and other muscles, induced by a profuse loss of blood during a menstrual period and by inability to retain food.* (See "Pernicious Anæmia.") 2. *Certain poisons,* especially phosphorus and arsenic, have a similar effect. In this group must be included poisons developed in the body in the course of acute infective diseases, especially diphtheria, in which a somewhat high degree of degeneration may be attained and be the cause of sudden death. 3. *Interference with the circulation in the coronary arteries* is also a frequent cause of a

* *Trans. Clin. Soc. Lond.*, vol. viii. 1875.

more or less general degeneration of the muscular tissue. This occurs especially in connection with aortic incompetence, and explains the early failure of cardiac power in this form of valvular disease. Atheromatous changes at the orifices of these arteries lead in the same way to diffuse fatty degeneration. Adhesive pericarditis and myocarditis act similarly; they hamper the heart mechanically, and the cause of the inflammation acts injuriously on the muscle-cells.

There is no clear line dividing the **circumscribed** from the diffuse form. Sometimes the degeneration, although perhaps more or less general, is much more advanced in some parts than in others. In such cases the heart presents a mottled appearance; opaque, pale yellowish or brownish patches are seen irregularly distributed throughout its substance. These patches, which vary considerably in size and form, are met with especially in the papillary muscles, the columnæ carneæ, and in the layers of fibres immediately beneath the endocardium. They may also occur beneath the pericardium, and in the deeper portions of the organ. They correspond with the most degenerated portions of the tissue. They are soft and flabby, and have a rotten consistence, tearing readily under the finger. Under the microscope, the fibres are seen to be in an advanced stage of fatty degeneration, the sarcolemmata containing molecules of fat and oil globules, which in many parts have escaped and lie free amongst the surrounding but less degenerated tissues (Fig. 14, *b*). These more localised degenerations are most common in old people, and usually result from considerable disease of many of the *small* branches of the coronary blood-vessels, and not from conditions of general anæmia. The peripheral layers of muscular tissue also frequently undergo extensive fatty degeneration as the result of pericarditis. The connection between these localised degenerations and the occurrence of rupture or of aneurysm of the heart is well known.

Brown Atrophy of the Heart.—Somewhat allied to, and occasionally associated with, fatty degeneration of the heart, is the condition known as brown atrophy. This consists in a gradual atrophy of the muscular fibres, together with the formation of granules of brownish-yellow or blackish pigment. These granules of pigment, which are probably the colouring matter of the muscle, are either grouped in clusters around the nuclei, or more generally distributed within the fibre. The fibres are frequently, at the same time, the seat of more or less fatty degeneration (Fig. 16). This change usually occurs as a senile one, or as a part of general marasmus from other

causes. It is also met with in some cases of cardiac hypertrophy. Its recognition is in most case impossible without the aid of the microscope.



FIG. 16. — *Brown Atrophy of the Heart.* Showing the granules of pigment and the atrophy of the fibres. The latter have in some parts undergone slight fatty metamorphosis. × 400.

Fatty Degeneration of the Kidneys.

Fatty degeneration of the kidneys frequently occurs as a result of inflammation of these organs. This **secondary** degeneration will be alluded to when treating of renal inflammations. **Primary** fatty degeneration is much less frequent. It must be borne in mind that the renal epithelium very commonly contains more or less fat; but it is only when this is excessive that it can be regarded as a diseased condition. This excessive formation of fat in the kidney is less common than is generally supposed. It is, however, occasionally met with in chronic diseases, especially in pulmonary phthisis. It is also a result of poisoning by phosphorus.

In simple fatty degeneration, the change is usually confined to the epithelium of the cortex. The cortex presents on section a somewhat yellowish-white surface, often slightly mottled, and this, in most cases, is most marked near the bases of the pyramids. There is no adhesion of the capsule or granulation of the surface. Microscopically only the nuclei of the vessels and of the connective-tissue stain well. This change appears to interfere but little, if at all, with the functions of the organs, and in this respect it resembles the analogous change in the liver. It is not usually accompanied by albuminuria.

Cerebral Softening.

This is, perhaps, the most suitable place to speak of cerebral softening, inasmuch as fatty degeneration of the brain-tissue usually constitutes a prominent feature in the histological changes. Softening of the cerebral substance is essentially a necrotic process and may result from any condition interfering with blood-supply—viz., inflammation, embolism, thrombosis of arteries or, much more rarely, of veins. Portions of the brain which are the seat of this change may be merely rather softer than the surrounding healthy tissue, breaking down more readily under a stream of water which is allowed to fall upon them, or

they may be completely diffluent. They are never distinctly circumscribed, but pass by insensible gradations into the neighbouring tissue.

Under the microscope, the change is seen to consist in a disintegration of the nerve-tissue. The fibres suffer earliest: their white substance first coagulates, and then breaks up into masses of various sizes, giving the reactions of fat: these give place to masses of fine fat-granules. These granules are for the most part the products of the degeneration of the myelin, and are due to the decomposition of lecithin, which is its principal constituent.

Next, when the grey matter is implicated, the large nerve-cells are involved in the necrotic stage, but though full of granules their outline may long remain visible. Lastly, the neuroglia-cells and those of the small bloodvessels degenerate similarly, and the tissue is thus converted into broken-down fibres, granular matter, and molecular fat, amongst which are many granule-cells (p. 51). These corpuscles are more common in cerebral softening (Fig. 17) than in any other condition; and form very characteristic objects: they vary from $\frac{1}{500}$ to $\frac{1}{2000}$ inch in diameter, and the granules they contain are possibly myelin but usually fat. Many are formed by degeneration of ganglion-cells and neuroglia-cells, but many—perhaps most—are leucocytes which have taken up granules. Ultimately all trace of structure is lost.

The colour of the softened portion varies considerably, chiefly with the amount of blood, in the vessels, or extravasated into the tissues. It may resemble that of the surrounding healthy tissue, or be of a yellowish or reddish tint. According to these variations in colour, cerebral softenings have been classified into **white**, **yellow**, and **red**. As, however, a yellow softening may be but a later stage of red, and as white may be succeeded by red due to hæmorrhage into the area, and again as softenings of inflammatory and of simple degenerative origin may be to the naked eye indistinguishable, this classification has little practical or scientific value.

White Softening is sometimes **acute**, and is then due to embolism of one of the larger arteries, and which usually soon causes death. Far more commonly it is **chronic**, occurring especially in the aged. It is then due to gradual narrowing of the arteries by chronic endarteritis (atheroma), often combined with senile impairment of the heart-force, as a subsidiary cause of the imperfect blood-supply. Narrowing of the arteries from syphilitic endarteritis will act similarly

in earlier life. The process is really one of simple necrosis—sudden or gradual: when it is gradual there is no reason for hæmorrhage, and even when it is sudden, hæmorrhage is often absent, for infarction is rare after embolism of the brain. When the blood-supply is suddenly cut off it might be expected that coagulative necrosis (p. 22) would occur: but it never does. The area is softened and untinged by blood involved; and presents either a dirty white colour, or looks exactly like the brain around it. This affected area may be merely softened or quite diffluent; it may result in a cyst of clear fluid *without any blood pigment in its wall,* or in a scar—the latter appearing at first as a mesh-work, the spaces of which are full of milky fluid. Before the circulation has ceased and the death of all the elements in an area of white softening is complete, a fattily degenerated vessel may burst into the area and transform it into one of red softening.

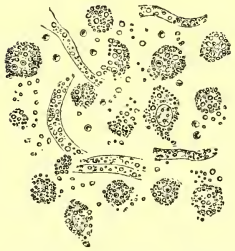


FIG. 17.—*Chronic White Softening of the Brain.* Granular corpuscles, broken-down nerve-fibres, and fat-granules, of which the softened substance is composed. The one or two nucleated cells are probably nerve-cells. × 250.

Red Softening is commonly dependent upon vascular obstruction, either from embolism or thrombosis. There is collateral hyperæmia, rupture of capillaries, and extravasation of blood; the softened tissue usually exhibits red points and patches mingled with white and yellow; the patch is swollen in proportion to the hæmorrhage and œdema, and is rarely diffluent. Red softening is most common in the vascular grey matter of the cortex and of the basal ganglia. Red softening is also sometimes associated with the chronic white variety. It may be inflammatory.

Yellow Softening is a later stage of red softening, and, like it, is usually situate in the grey matter—chiefly of the convolutions. The colour is due to the presence of altered blood pigment, the result of the previous extravasation. The pigment may be seen as fine dark granules and hæmatoidin crystals, scattered through the cells of the neuroglia and the nerve-cells of the grey matter; at first sight the granules look like fatty particles, but are distinguished by their dark black colour. White and yellow softening may remain unchanged for long periods.

CHAPTER IV.

CLOUDY SWELLING (Parenchymatous or Granular Degeneration, Albuminous Infiltration).

Cloudy swelling is a frequent change, being found in all diseases attended by considerable pyrexia. Wickham Legg and Liebermeister, having produced it by subjecting animals to a high external temperature, regarded the change as due simply to the fever, which, in their opinion, caused increased destruction of albumin. Increased destruction of tissue may, however, itself produce the elevation of temperature: moreover, the change is not most marked in long-continued secondary fevers, but in the relatively short primary fevers of the acute specific diseases. Further, the degeneration is specially pronounced in bad cases of diphtheria, in which disease the temperature is often low. All this leads to the belief that mere fever is an insufficient cause. A more probable explanation is that the infective material in the blood—the cause of the fever—has a more or less deleterious action on the tissues. This is supported by the observation that cloudy swelling is the first change noticeable in poisoning by phosphorus, arsenic, and the mineral acids, all of which lead ultimately to fatty degeneration of protoplasm. Again, cloudy swelling is found in inflamed parts, and we shall see, when considering inflammation, that it is always due to the action of an irritant, which, if it were of sufficient intensity, would produce death of the tissue. It would appear, therefore, that cloudy swelling is due to the action upon the tissues of some poison which *tends* to cause their death; elevation of the temperature of protoplasm above the normal would undoubtedly assist its action.

In considering the histology of this change, we shall find that advanced cloudy swelling passes insensibly into fatty metamorphosis: it is, therefore, to be regarded as *the first step towards fatty metamorphosis.*

SEATS.—The large masses of protoplasm show the change most plainly—the liver, kidneys, heart, and voluntary muscles; but probably all protoplasm suffers. The change may be much more advanced in some organs than in others, owing perhaps to differences in the local circulation.

APPEARANCES.—1. **Microscopic.**—The cells are swollen and their protoplasm is finely granular—the nucleus and any cell-structure being obscure or even indistinguishable: the granules refract light but

feebly ; they are unstained by osmic acid ; they dissolve in dilute acetic acid but not in ether, and are therefore albuminous. In advanced cases, larger, strongly-refracting granules, blackening with osmic acid, and soluble in ether but not in acetic acid—therefore fatty—are found associated with the albuminous granules which first appear like a precipitate in the cells.

2. **Naked Eye.**—When the change is well-marked, the affected organs are somewhat swollen, and may be either anæmic or slightly hyperæmic ; the surface of a section bulges up a little ; the tissue is softer and more opaque than natural.

EFFECTS.—This change must impair in proportion to its degree, the vital activity of the cell, on the other hand the affected parts completely recover in those cases in which the primary disease does not prove fatal. Of course its most serious action is upon the heart.

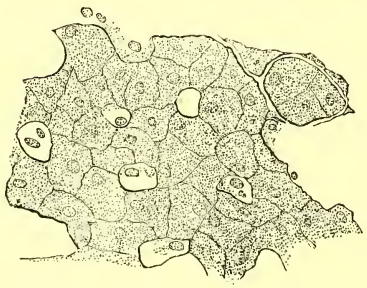


FIG. 18. — *Liver from a case of Acute Rheumatism with high Temperature.* The liver-cells swollen and granular, the nucleus in many being almost indistinguishable. × 200.

The Liver.—Here the change is usually most marked, and is absolutely characteristic (Fig. 18).

The Kidneys.—The cortex is principally affected. The Malpighian bodies and the pyramids are usually hyperæmic, and contrast with the general pallor of the cortex. The tubal epithelium presents the appearances above described ; they are well seen in the early stages of scarlatinal nephritis.

The Heart and Muscles.—The heart becomes slightly opaque, pale, and soft. The muscular fibres are finely granular, and have lost their distinct striation (Fig 19). Such a condition must materially interfere with the contractile power of the organ. A similar change is met with less frequently in other muscles.

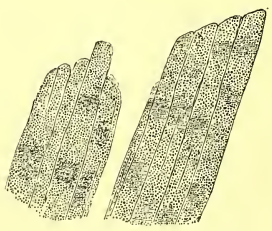


FIG. 19.—*Muscular Tissue of the Heart, from a Case of severe Typhoid Fever.* The fibres are granular, the nuclei obscured and the striation lost. × 400.

The Lungs.—The change cannot be recognised by the naked eye. The epithelial cells, according to Buhl, are swollen and granular from the presence of albuminous and fatty particles, and are easily detached from the alveolar walls.

CHAPTER V.

MUCOID AND COLLOID DEGENERATION.

Mucoid Degeneration.

Mucoid degeneration consists in the transformation of the proteid constituents of the tissues into **mucin**.

Chemically, mucin is closely allied to albumin, more so than to either gelatin or chondrin. Like albumin, it is met with only in alkaline fluids—being held in solution by the free alkali; it is precipitated by dilute acetic acid and alcohol. It differs from albumin in not containing sulphur, in being insoluble in an excess of the acid, and also in not being precipitated by boiling, by tannin, or by perchloride of mercury. These two reagents will distinguish it also from gelatin and chondrin, which are both precipitated by them.

CAUSE.—This is unknown. It appears to be a reversion to an earlier state; for, in the fœtus, the connective tissues consist almost entirely of soft mucin-yielding substance: the umbilical cord and vitreous humour retain this peculiarity. Throughout life a mucoid change occurs physiologically in the secretion of mucus; a clear drop of mucus appears in the protoplasm and increases till the cell bursts and the mucus is evacuated—the cell, as a rule, not being destroyed.

Myxœdema, a disease due to atrophy of the thyroid body, was so named because it was supposed that the swollen connective-tissue contained a large quantity of mucin. Recent observations, however, have shown that, at the time of death, the proportion of mucin in the skin is only slightly, if at all, in excess of the normal amount.

SEATS.—*Pathologically,* mucoid degeneration may affect both cells and intercellular substance. It is met with in catarrh of mucous membranes, the transformation occurring much more rapidly than

under normal conditions, and the cells being often cast off; also in connective-tissue, in cartilage (especially the intervertebral and costal cartilages of old people), in bone, and in many new growths, not only in those of the connective-tissue type, but in both cells and matrix of cancers.

APPEARANCES. — *Under the microscope* these are the same as in the physiological process, but the cells are much more frequently destroyed. *To the naked eye* the affected parts are transformed into a homogeneous, colourless material, of a soft, mucilaginous, jelly-like consistence. When the change is limited to isolated portions of the tissue, the softened parts surrounded by those which are unaltered, often present the appearance of cysts. These cyst-like formations containing mucoid substance are not uncommonly met with in the costal cartilages and in new growths.

EFFECTS. — Complete mucoid degeneration implies abolition of function.

Colloid Degeneration.

Colloid degeneration consists in the metamorphosis of cell-protoplasm into a substance known as "**colloid.**"

Chemically, colloid differs from mucin in containing sulphur and in not being precipitated by acetic acid or alcohol. It swells when treated with acetic acid.

In the adult many vesicles of the thyroid normally contain colloid; it is only when the formation of this material becomes general and excessive, producing one form of goître, that the process is to be regarded as pathological.

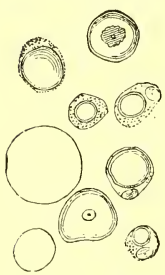


FIG. 20. — *Colloid Cells*, from a colloid cancer (Rindfleisch).

CAUSE.—This is quite unknown.

SEATS.—Colloid degeneration occurs most often in the thyroid; then in certain new growths—both sarcomata and cancers: the secondary growths in glands and elsewhere undergo the same change. It must be remembered that the term "colloid tumour" implies nothing as regards the nature of the growth. Ovarian tumours often contain "colloid;" but sometimes the contents more nearly correspond to mucin. Other seats are rare.

APPEARANCES.—1. **Microscopic.**—(Figs. 20 and 21). One or two small masses of colloid appear in the cell, increase and push aside the nucleus until they have replaced all protoplasm and the cell is considerably swollen. The nucleus usually atrophies and disappears, but may become colloid. Neighbouring cells coalesce into small masses, and these again into larger, which not uncommonly, under the microscope, look as if they were concentrically laminated

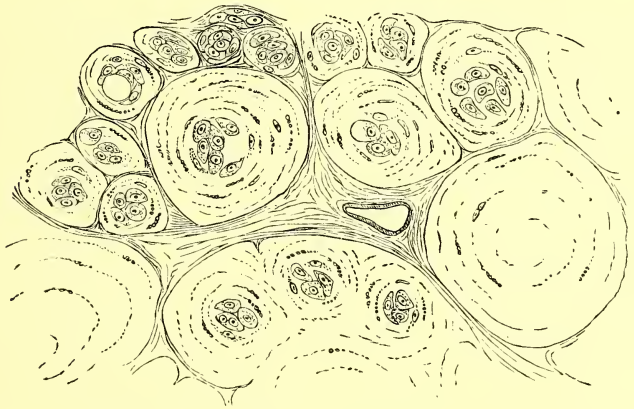


FIG. 21.—*Colloid Cancer.* Showing the large alveoli, within which is contained the gelatinous colloid material. × 300. (Rindfleisch.)

(Fig. 21). Thus cavities full of colloid are formed. The intercellular substance atrophies rather than degenerates, whilst in mucoid degeneration it is frequently affected by the morbid process.

2. **Naked Eye.**—Colloid is colourless or pale yellow, glistening, and has the consistence of rather soft gelatin, which, indeed, it much resembles. Quite small points of colloid catch the eye; they do not stain characteristically with iodine or the aniline dyes. The physical characters of colloid tissues are thus very different from those of mucoid tissues. In advanced stages, however, colloid may soften; and masses of softened colloid separated by septa of comparatively undegenerated tissue give the appearance of cysts in a tumour.

EFFECTS.—Abolition of function is proportionate to the extent of the metamorphosis.

Zenker's Degeneration of Muscle.

This change has been regarded as allied to colloid degeneration; but its nature is doubtful. It was first described by Zenker as occurring in the muscles in typhoid, and chiefly in the recti abdominis, adductors of the thigh, the diaphragm and tongue-muscles. It is now known to occur, though less often, in other infective febrile diseases, such as small-pox and cerebro-spinal meningitis; in trichinosis; also in the neighbourhood of burns, bruises —either before or after systemic death—abscesses and tumours of muscle. Probably, as Cohnheim suggested, the unusual appearance of muscle thus affected is due to a disturbance in the ordinary post-mortem coagulation of myosin: in other words, "Zenker's degeneration" is an example of coagulative necrosis. The appearances may certainly be produced after systemic death, and may almost certainly occur during life in individual fibres dying from any cause.

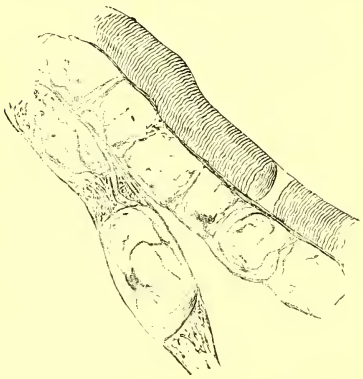


FIG. 22.—*A Portion of the Soleus Muscle from a Case of Typhoid Fever.* Preparation teased after treatment with Müller's Fluid. × 200. Reduced ⅓.

APPEARANCES.—The altered fibres are much swollen and the transverse striation is lost. The sarcolemmata are occupied by a homogeneous, structureless material, which is exceedingly brittle, and usually presents a wrinkled appearance, or is broken up transversely into several irregular fragments (Fig. 22).

The portions of muscle affected are, to the naked eye, semi-opaque, pale, slightly lustrous, of a reddish-grey or brownish-yellow colour, and abnormally friable. They appear somewhat like the muscles of frogs or of fish. The fibres are never universally affected; many normal are found associated with the altered elements.

EFFECTS.—This change necessarily impairs the contractile power of the muscle, and it is believed often to lead to rupture of some of the fasciculi and to hæmorrhage. The dead fibres appear to be readily absorbed and quickly regenerated.

Hyaline Degeneration.

This name was given by v. Recklinghausen to a morbid change characterised by the presence in cells of drops of a substance having an appearance like that seen in albuminoid degeneration, but not giving the colour-reactions of the latter. It is stained pale yellow by iodine, and in other respects seems allied to "colloid." It is said by v. Recklinghausen to be a normal constituent of cell-protoplasm, and to be set free when the cell dies. Very little is known about the substance, however, and there is a tendency on the part of some writers to include under this heading all morbid changes resulting in a hyaline appearance, and especially those due to coagulative necrosis.

The chief seats of this change appear to be the arteries of the brain and of lymphatic glands; in arterioles the adventitia is converted into a shining thickened layer. In larger arteries becoming aneurysmal, Meyer has described the yielding as being due to hyaline degeneration starting internally and passing outwards. The same degeneration is said to be frequent in inflamed parts, the connective-tissue being affected. Gull and Sutton have described a hyalin-fibroid change in the arteries in chronic Bright's disease.

CHAPTER VI.

LARDACEOUS DEGENERATION.

Syn. Waxy, Albuminoid, or Amyloid Degeneration.

This, which is one of the most important degenerative processes, is characterised by the appearance in the tissues of a colourless translucent, firm lardaceous substance, giving them somewhat the appearance of boiled bacon or of white wax. This substance offers an exceedingly prolonged resistance to gastric digestion, and exhibits some remarkably characteristic staining reactions. The reaction with iodine led Virchow, its discoverer, to regard the substance as allied to starch and to propose for it the name "amyloid substance."

Chemical nature of the new material.—By submitting affected organs to gastric digestion the substance may be obtained practically

pure; and, thus obtained, it has been shown by Kühne to be nitrogenous, closely allied to albumin, and not starchy. It is distinguished from albumin chiefly by its resistance to the action of (1) dilute acids and alkalies, (2) the gastric juice at the body-temperature, and (3) putrefaction; also by certain colour-reactions. Marcet has shown that the organs containing it are notably deficient in potassium and phosphoric acid, but they contain excess of sodium and chlorine.

With regard to its **colour-reactions** the best and longest known is that with iodine. To obtain this, wash a thin slice of an affected organ thoroughly to free it from blood, and then pour over it a watery solution of iodine, made by diluting one drachm of liquor iodi with seven of water. In this way the lardaceous portions are quickly stained dark mahogany brown, the healthy tissues assuming a bright yellow colour.

If this stained surface be treated with a ten per cent. solution of sulphuric acid, degenerated parts assume, either at once or after some time, a dark greenish, bluish or blackish hue, whilst healthy parts become greyish. Unfortunately this second reaction is very variable and of little value.

For microscopic purposes the iodine and sulphuric acid reaction may be obtained by staining the sections with iodine, mounting them in glycerine and placing at the edge of the cover-glass a very small quantity of strong sulphuric acid; in about 24 hours, the lardaceous tissues will be found stained blue. But a more valuable, though still somewhat variable process, is that of staining the sections with methyl aniline or gentian violet (1 per cent. watery solution); after some hours, the degenerated parts are stained bright magenta, but the healthy, blue. This staining is more permanent than that by iodine, and is valuable as a confirmatory test; for the iodine reaction may be obtained with glycogen and some forms of altered albumin, and cannot therefore be regarded as absolutely characteristic of lardaceous degeneration.

ÆTIOLOGY.—Lardaceous degeneration is said to be much commoner in males than in females, and the ages of the great majority of patients fall between 10 and 30, especially between 20 and 30. It is almost always *secondary* to prolonged and profuse suppuration, due usually to tubercular disease of lung, bone, joint, or kidney, but sometimes to traumatic (septic compound fractures) or other causes (dysentery, actinomycosis). Much less commonly it is found in the

cachexia of tertiary syphilis, especially when there is chronic bone-disease. Rarely it appears in the cachexiæ of severe malaria, of leukæmia and of cancer; and very rarely, especially in children, the degeneration may seem to be *primary*. Most of these diseases belong to the class of infective diseases, and Birch-Hirschfeld suggests that the degeneration may be due to an infective cause—but he adduces no evidence in favour of this.

The degeneration may be very rapid (two to three months, Cohnheim) in appearing, or, under apparently similar circumstances, its onset may be long delayed; this is more likely to be the case in young children than in adults. Like hectic fever, this degeneration occurs much more readily from suppuration of foul, ill-drained cavities than from a much more free discharge from a cutaneous ulcer—upon which the pus cannot accumulate under pressure.

SEATS.—The change is almost always widely distributed: only rarely is it limited to a single part. It may be found in almost any organ; those most frequently affected are **spleen**, **liver**, **kidneys**, **intestines**, and **lymphatic glands.** Less frequently, and especially when the change in the organs just mentioned is advanced, minor degrees of it may be found in the stomach, supra-renal capsules, pharynx, œsophagus, bladder, prostate, generative organs, serous membranes, the membranes of the brain and cord, and muscle. There is no rule as to the order in which the organs are affected, nor as to which will be affected in any given case. As a **local change**, apparently quite distinct from the condition indicated by "lardaceous degeneration," it occasionally affects *pathological products*, as old thrombi, inflamed glands, scars (especially syphilitic) and tumours.

APPEARANCES.—1. **Microscopic.**—The morbid substance usually appears first in the sub-endothelial connective-tissue of the **arterioles** and **capillaries**, and in the media of the former; the endothelium is unaffected, and the adventitia usually escapes. The change greatly diminishes the lumen of the vessel; it does not affect the latter uniformly, but frequently causes spindle-shaped enlargements; and not only do the vessels of many parts escape entirely, but the distribution of the change in an affected organ may be quite irregular.

With regard to the further spread of the change, all authorities of recent date appear agreed that the *connective-tissue* in every affected

organ suffers most, and swells into homogeneous waxy-looking masses, frequently coalescing, between which the essential cells of the organ atrophy even to disappearance. With osmic acid and ordinary staining reagents, Ziegler says that there is no difficulty in demonstrating the fatty liver-cells between the homogeneous blocks into which the connective-tissue has swollen (Fig. 23, from Rindfleisch, and said by him to represent degenerate liver-cells). Many writers, in opposition to the old view, now deny that epithelial cells can undergo this change; though others, like Ziegler, content themselves with saying that they may be quite unaffected in advanced stages of the disease. Opinions differ as to whether muscle-cells and those of lymphatic glands become lardaceous.

2. **Naked Eye.**—Organs in which this change is at all advanced present features so characteristic that its nature can be readily recognised by the naked eye. They are considerably increased in size, but their general form is preserved, any edges becoming more or less rounded. Their absolute weight is increased, and also their specific gravity; their surface is smooth, and the capsule tense and stretched; their consistence is firm and somewhat elastic. On section they exhibit a peculiar homogeneous, glistening, translucent appearance, somewhat resembling pure white wax. Owing to the diminished calibre of their blood-vessels, and to the pressure exercised by the new material, they contain but little blood, and hence are always pale in colour. In slighter degrees of the change, spots and patches of the morbid material may be scattered, like grains of boiled sago, through the tissue. Although the above characters are sufficient in advanced stages, the colour-reactions already mentioned should always be used, for they will reveal altered patches—*e.g.*, in intestine—not obvious without them. For the recognition of the degeneration in its *earliest* stage the microscope is necessary. *The presence of lardaceous degeneration is often marked by some other change, especially fatty.*

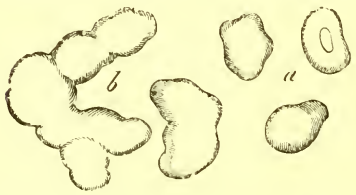


FIG. 23.—*Lardaceous Liver Cells* (according to Rindfleisch). *a*. Single cells. *b*. Cells which have coalesced. × 300. Probably the above masses are fragments of capillaries or of connective-tissue.

The primary change may occur in the connective-tissue of an organ, and not in the vessels.

EFFECTS.—The result of diminishing the blood-supply to the essential elements of a part by narrowing the arterioles, and by direct pressure on the elements, is naturally to cause atrophy, frequently accompanied by fatty degeneration (p. 33); and proportionate diminution of function follows. The change in the vessel-walls alters the quantity and quality of the transudation, as is shown by the changes in the urine when the kidneys are affected.

It seems probable that removal of the cause—*e.g.*, chronic suppuration—of lardaceous degeneration may lead to arrest of the deposit, and to its removal from the diseased organs, even in marked cases; but in the great majority of instances the change is steadily progressive, and proves fatal by exhaustion, preceded by anæmia, hydræmia, albuminuria, and diarrhœa—all of which are easily accounted for by the morbid anatomy. But the other effects of the *primary* disease must also be remembered.

NATURE OF THE DEGENERATION.—Is the process an infiltration or a metamorphosis? It is generally regarded as an infiltration; and it is believed that a soluble lardaceous substance is deposited from the blood in tissues predisposed by some morbid change to receive it and to combine with it to form the very insoluble "lardacein" or "lardaceous substance," found in the organs. The latter change accounts for the irregular distribution of the degeneration. A parallel was drawn by Virchow between this degeneration and calcareous infiltration, in which the deposit of salts occurs only in dead tissues. The nature of the process is, however, by no means certain, some facts supporting the view that it is a metamorphosis—*e.g.*, the occurrence of the lardaceous substance in thrombi, and perhaps in casts.* Dickinson maintains that the substance deposited from the blood is de-alkalised fibrin, rendered insoluble by loss of alkali carried away in the pus. But this explanation fails to cover many cases, and Budd considers that such a substance should digest easily.

Seegen thought he found in normal blood a substance named "dystropodextrin" which has the peculiarities of the lardacein; he believes that this substance loses its solubility and is then deposited.

According to Kekule and others, lardacein is a possible intermediate product between albumin on the one side, and fat and cholesterin on the other.

* P. 77.

Lardaceous Degeneration of the Liver.

APPEARANCES.—1. **Microscopic.**—The change usually begins in the walls of the capillaries and arterioles of the hepatic artery; rarely, it is said, in the capillaries of the portal vein. Thence the deposit spreads to the intra-acinous connective-tissue round the affected vessels, ultimately reaching and affecting the tissue between the lobules and leading to confusion of their outlines. The connective-tissue swells into homogeneous columns which split readily into flakes,

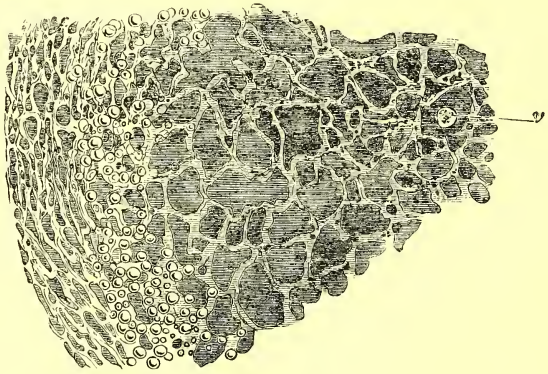


FIG. 24.—*Lardaceous Liver.* Part of a lobule, showing masses of lardaceous substance, resembling in section degenerate and fused hepatic cells, and greater implication of the intermediate zone. Externally are seen several fatty cells, a certain amount of fatty infiltration being associated with the lardaceous change. *v.* Hepatic vein. × 100.

like hepatic cells, and which, in section, look like masses of degenerated cells or even whole lobules. Careful examination (p. 70) will, however, reveal between the lardaceous masses the liver cells more or less atrophied and pigmented, the peripheral cells, especially, being infiltrated with fat. These changes are beautifully shown if a very thin section be dehydrated in absolute alcohol, stained in an alcoholic solution of alkanet, decolorised in alcohol acidulated with hydrochloric acid, washed in water tinted with acid hæmatoxylin, again washed in water coloured with solution of iodine and iodide of potassium, once more rinsed in water, and then mounted in glycerine; the fat is bright red,

the lardaceous substance brownish-red, the liver cells yellow, and the nuclei dark greyish-blue. The fatty liver cells show up clearly between the lardaceous masses, especially if a condenser is used (Orth).

2. **Naked Eye.**—The lardaceous liver is increased in size, and may be so large as almost to fill the abdominal cavity. Its weight is increased, and also its specific gravity. The enlargement being uniform the natural shape of the organ is but little altered; the free edge is rounded, the surface smooth, and the capsule tense and stretched. The consistence is firm and elastic. The cut surface is dry, bloodless, smooth, translucent, and waxy-looking, and of a pale reddish-grey or dirty-yellow colour. If the change is very far advanced, the tissue may be perfectly homogeneous, all distinction between the individual lobules being lost. In other cases the lobules are distinctly mapped out; they are enlarged, and the external zone may be of an opaque yellowish-white colour owing to the presence of fat. This association of the fatty and lardaceous changes is exceedingly common. Lardaceous degeneration does not obstruct the portal circulation, and hence does not cause ascites (see "Cirrhosis of Liver"). It causes fatty degeneration and atrophy of the hepatic cells, and thus interferes with the functions of the organ.

If thin washed sections of a liver in an early stage of the affection be stained with iodine, the mahogany colour will be found limited to the so-called "intermediate zone" of the lobules—the area of distribution of the hepatic artery. The appearance thus produced is that of a number of partially compressed rings with pale centres, and still paler intervening spaces (Fig. 25). The earliest seat of lardaceous degeneration thus differs from that of fatty infiltration, in which the fat first accumulates in the cells of the outer or portal zone (Fig. 24), and also from that of pigmentation of the hepatic cells from mechanical congestion, which begins in the central zone around the hepatic vein. All these changes not uncommonly occur together. As the lardaceous change advances, the whole lobule and the interlobular connective-tissue may become involved.

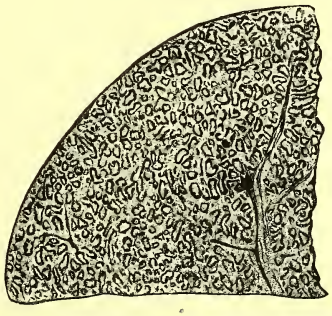


FIG. 25.—*Lardaceous Liver.* Stained with Iodine. The darkest portions represent the affected intermediate zones. Natural size.

Lardaceous Degeneration of the Kidneys.

The kidneys suffer frequently from this change, though the spleen and liver are, as a rule, more markedly affected. Sometimes the degeneration appears to commence in the kidneys. Albuminuria being one of the most constant signs of this change, it is often classed as one of the varieties of "Bright's disease."

The combination of lardaceous and fatty changes is exceedingly common in the kidney, the latter being to some extent secondary to the former, but the two bear no constant or proportionate relation. Lardaceous change is also frequently combined with the signs of inflammation, both interstitial and parenchymatous: the nature of the relation is sometimes obscure. It has been held that the nephritis causes the lardaceous change, that the lardaceous change causes the nephritis, and that both are concomitant results of the same cause.

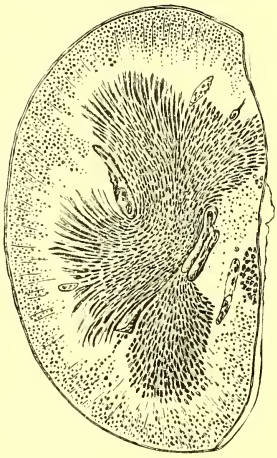


FIG. 26. — *Lardaceous Kidney.* Stained with Iodine. The dark parts represent the Malpighian bodies and arteries which have undergone the lardaceous change. From a child. Natural size.

APPEARANCES. — 1. **Microscopic.**—The degeneration usually begins in the Malpighian bodies. At first only a few of the capillary loops in each tuft are affected, but all the loops gradually become involved. The whole coil then presents an ill-defined outline and glistening surface. The change in the meantime extends to the afferent arteries, to the capillary network around the tubules, to the arteriolæ rectæ of the medulla, and in advanced cases to the intertubular tissue, and even to the tunica propria of the tubules. It is doubtful if the epithelium *ever* undergoes lardaceous change. The distribution of the change may for long be very irregular.

The minute changes are first observed in the sub-endothelial connective tissue, the endothelium remaining sound; the media of the arterioles is next involved, the muscular fibres either atrophying or degenerating; in this way a homogeneous glistening layer of varying thickness (Fig. 27) is formed. The lumen of the vessels is finally

obliterated, and the enlarged Malpighian tuft becomes a solid ball, bearing on its surface the unaffected epithelial cells of its capsule: these can be demonstrated by ordinary staining reagents. From the Malpighian tufts and afferent vessels the degeneration spreads as above described, giving rise to the dots, streaks and finally coalescent patches presently to be described.

At first the tubes and their epithelium appear normal. Many contain the pale hyaline casts which appear in the urine. These are probably simple exudation products, but they occasionally stain deep brown with iodine, and thus have been supposed to consist of lardaceous substance formed by metamorphosis of the exudation

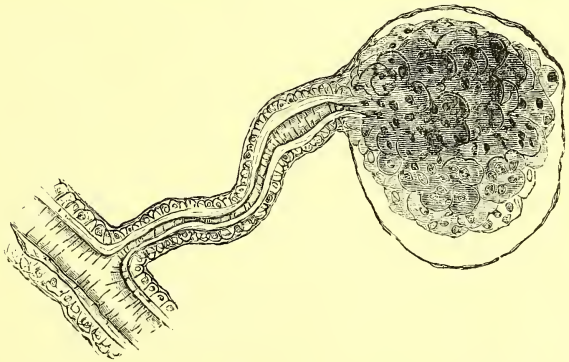


FIG. 27. — *Lardaceous Degeneration of a Malpighian Tuft and small Artery of the Kidney.* Showing the thickening of the walls of the vessel, the enlargement of the cells of the circular muscular coat, and the homogeneous layer formed by the intima and longitudinal muscular fibres. × 200. Reduced ⅓.

material; according to Ziegler, however, these casts do not exhibit the other reactions of lardaceous substance. As the change advances and the new material increases in amount, the blood-supply becomes less and less, while the tubes themselves are subjected to actual compression which, if it is uniform, leads to their atrophy, and perhaps even to their disappearance, and if it is irregular, to their dilatation into small cysts. The epithelium undergoes atrophy and fatty metamorphosis, producing the opaque yellowish streaks and patches above mentioned, but this change varies much in its amount and distribution. Not uncommonly a parenchymatous nephritis is present, the tubes being distended with cloudy or fatty cells, and the intertubular tissue being more or less infiltrated with leucocytes (*large white lardaceous kidney*).

In the later stages of the process there is almost always increase of the intertubular tissue, which, together with the disappearance of tubes, leads to shrinking and toughening of the organ, to adhesion of the capsule and to irregularity of the surface.

2. **Naked Eye.**—These will vary with the extent of the degeneration, and may be modified by the presence of associated changes, such as fatty degeneration of renal epithelium, and of those due to inflammatory processes.

At first the changes are microscopic only; at this stage the staining of thin sections with iodine will show here and there a Malpighian body as a brown dot, and the straight arteries of the pyramids as brown lines. The unstained kidney is either still normal to the naked eye, or perhaps pale, yellowish, and slightly softened. As the disease advances, the organ enlarges, especially the cortex. The surface is to the naked eye smooth, and the capsule separates readily. The enlarged cortex is remarkably pale and anæmic, and has a peculiar translucent, homogeneous, wax-like appearance. Its consistence is hard and firm. A few scattered vessels may be seen on the surface, and the bases of the pyramids sometimes exhibit increased vascularity. If iodine be applied to the cut surface (p. 70), the Malpighian bodies and the arteries of the cortex become mapped out as clearly as in an artificial injection (Fig. 26). The enlarged Malpighian bodies may indeed be seen as glistening points before the iodine is applied. Frequently, the homogeneous appearance of the cortex is interrupted by minute, opaque, yellowish-white lines and markings; these are produced by the fatty changes in the epithelium of the tubes, already described. Ultimately the capsule becomes more or less adherent, and slight irregular depressions make their appearance upon the surface of the organ; the latter are due to atrophic changes in some of the tubes. If, as is usually the case, the process is associated with an increase in the intertubular connective-tissue, the atrophy may render the organ even smaller than normal.

Sometimes the enlargement of the organs is very great. In these cases the increase in size is mainly due to inflammatory changes, such as have been referred to. The frequency with which such combinations occur render it advisable to examine all large pale kidneys for lardaceous changes.

EFFECTS.—The first effect of this change is to obstruct the circulation in the cortex: hence the increasing pallor of this part. The

arterial walls are so altered that fluids and albumin readily permeate them; and thus is produced the large quantity of urine, loaded with albumin, which characterises the earlier stages of this affection; the polyuria is, however, not so great as in the granular contracted kidney, in which the arterial tension is much higher. It is unusual to find the heart hypertrophied in cases of lardaceous disease. As the arteries and the tubes become more obstructed, the urine diminishes in quantity. The excretion of urea is less interfered with than in other forms of Bright's disease, and hence symptoms due to its retention seldom occur. Tube-casts are rarely numerous; they are for the most part hyaline or finely granular, though sometimes they are covered with fatty epithelium.

In advanced cases there is marked dropsy.

Lardaceous Degeneration of the Spleen.

VARIETIES.—The spleen is very liable to this change, and is usually one of the first organs to be affected by it. Two forms are

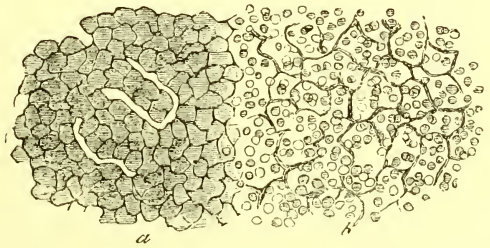


FIG. 28.—*Lardaceous Degeneration of the Spleen—"Sago Spleen."* Part of an altered Malpighian corpuscle, *a*, with the adjacent normal splenic tissue, *b*. The canals in *a* are degenerated vessels. × 200.

generally described: (1) the **sago** spleen, in which the disease is limited to the Malpighian corpuscles; and (2) the **diffuse** form, in which the whole splenic pulp is implicated, but in which the Malpighian corpuscles generally escape. Kyber speaks of the latter as "parenchymatous degeneration," and makes a third form, indistinguishable from it by the naked eye, in which the disease begins simultaneously in the Malpighian corpuscles and the pulp. He holds strongly that these forms do not pass into each other, and particularly that the parenchymatous form is not an advanced stage of the sago spleen.

APPEARANCES.—1. **Microscopic.**—In the **sago** spleen the change commences in the capillaries and arterioles of the Malpighian corpuscles, next involves the fibrils of the network of which the corpuscle largely consists, and then extends to the small vessels in the neighbourhood. At first the central artery of the corpuscle usually escapes. When it becomes affected, the change is first observed in its middle coat. In the **diffuse** or **parenchymatous** form, the degeneration begins in the neighbourhood of the capillary veins of the pulp, and spreads thence to the trabeculæ, arterial capillaries, and possibly—though this is very doubtful—to the cells. The Malpighian bodies often escape, but their central arteries are generally involved. Kyber's **general lardaceous degeneration** shows the lesions of both the other forms progressing simultaneously.

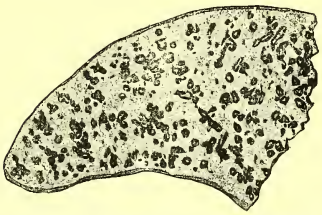


FIG. 29.—*Lardaceous Sago Spleen.* Stained with Iodine. Malpighian bodies are darkly stained, and as a rule have unstained centres. From a child. Natural size.

2. **Naked Eye.**—The **sago spleen** is more or less enlarged; its weight and density are also increased. The cut surface is smooth, dry, and studded all over with small glistening sago-like bodies, varying in size from a millet to a hemp seed. These are stained reddish-brown by the iodine solution; but, as the central artery generally escapes, the mahogany-coloured nodules have pale centres. These nodules may enlarge until they occupy a considerable portion of the organ, although in earlier stages of the affection they are so minute that they can be seen only in thin sections of the tissue. In the later stages, therefore, there is a considerable resemblance between iodine-stained sections of liver and spleen respectively, as may be seen by comparing Figs. 25 and 29.

In the **parenchymatous** and **general forms** the organ often attains a much larger size than is met with in the sago spleen. It is remarkably hard and firm, and the capsule is tense and transparent. On section it presents a dry, homogeneous, translucent, bloodless surface, of a uniform dark reddish-brown colour. Thin sections can be readily made with a knife, the organ cutting like soft wax. The corpuscles, if affected, are not visible as in the former variety, being probably obscured by the surrounding pulp.

EFFECTS.—Anæmia and emaciation follow the interference with the blood-forming function of the spleen.

Lardaceous Degeneration of Lymphatic Glands.

In the lymphatic glands the process much resembles that in the spleen. The small arteries in connection with the follicles of the gland are the earliest seats of the change; and from these it extends to the trabeculæ and possibly to the lymphoid cells. The follicle thus becomes ultimately converted into a small homogeneous mass.

The glands themselves are enlarged, and on section the minute wax-like bodies can often be seen scattered through the cortex. The cut surface is smooth, pale, and translucent.

The effects are the same as in implication of the spleen.

Lardaceous Degeneration of the Alimentary Canal.

The whole alimentary tract may be affected, but probably never primarily or alone. The change frequently co-exists with tubercular ulceration. The disease in this situation is very apt to escape observation, as it usually produces but little alteration in the appearance of the parts. The mucous membrane may look somewhat pale, smooth, translucent, and œdematous; in very advanced cases there may be some rigidity and thickening of the bowel-wall, and even ulcers—due, it is supposed, to the tearing-off, by the passing of food, of rigid villi. But the effect of the application of iodine to the washed mucous surface is very characteristic. In the small intestine—perhaps the part most commonly affected—a number of small reddish-brown points appear over the whole surface of the membrane; these correspond to the intestinal villi, the arteries and capillaries of which have undergone the lardaceous change. In the stomach and œsophagus the vessels are similarly mapped out by iodine (p. 70).

The change in the intestine gives rise to serous diarrhœa, probably due to increased permeability of the degenerated vessel-walls. Both absorption and secretion are much impaired, so that implication of the alimentary tract has a grave general effect.

The Corpora Amylacea.

Corpora amylacea or "amyloid bodies" were formerly looked upon as consisting of lardaceous substance; there appears, however, with

the exception of a certain similarity in their behaviour with iodine and sulphuric acid, to be no connection between them.

They are round or oval bodies, formed of a succession of concentric layers, and are often changed to a deep blue colour by iodine, thus bearing, both in structure and chemical properties, a strong resemblance to granules of vegetable starch (Fig. 30); but, sometimes, the blue is exhibited only after the subsequent addition of sulphuric acid, and thus a resemblance is shown to the lardaceous substance. Many of these bodies, however, are coloured green, or even brown by these reagents. The green is due to their admixture with nitrogenous matters, which give a yellow colour with iodine, and hence the combination yields a green. The greater the amount of nitrogenous matter the more brown does the colour become. They vary in size from microscopic granules to bodies which are distinctly visible to the naked eye; sometimes being as much as one or two lines in diameter. The larger are usually formed by the conglomeration of smaller granules, which are often enclosed by a common envelope.

They especially occur in conditions of atrophy or softening of the nervous system. The ependyma of the ventricles, the white substance of the brain, the choroid plexus, the optic nerve and retina, and the spinal cord are their favourite seats. The larger forms are met with most frequently in the prostate. The prostate of nearly every adult contains some of these bodies; and they may accumulate in that organ to such an extent as to form large concretions. They are occasionally met with in the lungs, and in mucous and serous membranes.

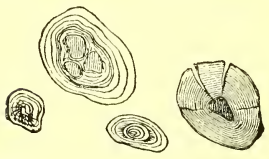


FIG. 30. — *Corpora Amylacea from the Prostate.* (Virchow.)

From their laminated structure these bodies would appear to be formed by the precipitation, layer by layer, of some material, upon the surface of pre-existing particles. The material, however, does not appear to be that met with in lardaceous degeneration. The two processes are so different, both in the circumstances under which they occur and in the characters and seat of the morbid products, that they cannot be looked upon as analogous. Lardaceous degeneration is a general change, whereas the formation of the corpora amylacea is evidently of a local nature. The latter is often preceded by those local atrophic changes associated with advanced life, and appears to consist in the deposition of some material, probably liberated in the tissues themselves, upon any free body which may exist in its vicinity.

The corpora amylacea, especially those occurring in the choroid plexus and in the lateral ventricles, are very liable to become calcified, and they then constitute one form of "brain sand," which is so often met with in these situations.

CHAPTER VII.

CALCAREOUS DEGENERATION.

Calcareous *Degeneration* or *Calcification* consists in the *infiltration* of tissues with calcareous particles. It is a purely *passive* process, the cells taking no part in it; the tissue is gradually petrified, by the deposit of earthy salts from the blood—for their quantity greatly exceeds that present in healthy tissues. It is difficult to find a physiological type, but perhaps the deposit of earthy salts in the walls of the primary areolæ (see "Rickets") in a growing long-bone may be regarded as such. *Ossification* is quite distinct from *calcification*, for in it everything points to life and growth; the cells are undergoing *active* changes, and are obviously concerned in receiving the salts from the lymph and in combining them most intimately with the organic matrix.

ÆTIOLOGY.—Earthy salts in solution, chiefly the *phosphates* and *carbonates of calcium and magnesium*, are brought to the part by blood and lymph, carbon dioxide being probably the solvent. We have to determine why these salts should be permanently deposited in certain tissues, and we are at once struck by the fact that, in the immense majority of cases, the tissues affected are dead or dying. It is probable, therefore, that feeble nutritive activity and a retarded blood-stream are together responsible for its occurrence. Rindfleisch taught that carbon dioxide escaped from the stagnating lymph-stream, and that the earthy salts were consequently precipitated; more recently others have held that calcification is due to a combination of these salts with certain albuminoid bodies and with fatty acids.

Much more rarely calcareous infiltration appears to be due to an absolute increase of calcareous salts in the blood, such as may be supposed to occur in extensive caries and in osteomalacia. A portion of the excess is then deposited more or less widely in the tissues—first in the lymphatic glands and kidneys, more rarely in the lungs, stomach.

intestines, dura mater, and liver. The deposit takes place chiefly in the connective and least active tissue of the organ, which, moreover, immediately surrounds the vessels—*e.g.*, in the interlobular tissue of the lungs and in the stroma between the glands of the stomach; but in the kidney the epithelium is infiltrated as well as the intertubular tissue. Analogous to this form of calcification is the deposition of the excess of bi-urate of sodium which takes place in gout. It is probable that in this case also the deposit occurs first in tissues in which the nutritive activity is most feeble. A certain amount of chalky—like fatty—infiltration may perhaps occur without marked impairment of function; but, as completely calcified parts are certainly dead, either the infiltration has the power to kill or it affects dying parts.

SEATS.—Diminution or extinction of vital activity being an important element in its causation, we are not surprised to find that calcification is very common as a senile change, affecting most frequently the arteries and hyaline cartilages—excepting articular cartilages. It occurs similarly in pathological tissues of which the life is feeble—*e.g.*, in uterine myomata after the climacteric and in old scars. Lastly, dead tissues locked up in the body are very likely to become calcified—*e.g.*, thrombi (*phleboliths*), parasites (Fig. 31), atheromatous patches in arteries, and caseous masses—the results of arrested tubercular inflammation—so common in lungs and lymphatic glands. The best example is the complete calcification of a dead fœtus, which sometimes occurs when this is retained in the abdomen, in the case of an extra-uterine fœtation (*lithopædion*).

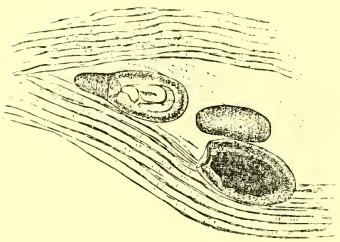


FIG. 31.—*Calcified Trichinæ in Muscle.* In two of the parasites the capsule and contents are so far calcified that hardly any trace of the coiled embryo remains. In the other the trichina is dead, shrivelled and becoming infiltrated. × 30.

APPEARANCES.—1. **Microscopic.**—The calcareous particles make their appearance both within the cells and in the intercellular substance; they are much more frequent, however, in the latter situation. They are seen at first as very fine dust scattered irregularly through the intercellular substance (Fig. 32). They are characterised, when viewed by transmitted light, by their opacity, black colour, irregular

outline, and solubility in dilute mineral acids, usually with evolution of bubbles of carbon dioxide. They gradually increase in number until ultimately large tracts of tissue may be converted into an opaque calcareous mass, in which the cells are enclosed and can no longer be recognised. These larger masses have a sharp black irregular outline, and as the calcification becomes complete, acquire a homogeneous, glistening, semi-transparent appearance. The cells themselves are much less frequently infiltrated, being merely enclosed and obscured by the calcified intercellular substance. Calcareous particles may,

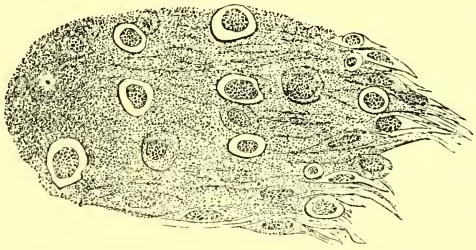


FIG. 32.—*A Calcified Sarcoma.* Minute calcareous particles are scattered through the intercellular substance; on the left so thickly as to almost conceal the cells. × 200.

however, make their appearance in the protoplasm, and, gradually increasing, convert the cell into a homogeneous calcareous body. Calcification of ganglion cells alone is not uncommon in degenerative processes in the brain.

If the saline matters are dissolved out with a little dilute mineral acid, the structure of the part may be again recognised, unless, indeed —as is so often the case—it has been destroyed by some antecedent change.

2. **Naked Eye.**—Apart from the microscope, calcification can be recognised more readily by touch than by sight. If the calcareous particles cohere in minute groups, such as is common when the process succeeds that of caseation, a white mortar-like substance is produced. When the cohesion is more marked, the deposit is comparable to fine sand; and all stages between this and solid stony masses may not infrequently be met with. The latter break with an irregular surface and present a yellowish or greyish aspect.

EFFECTS.—A calcified part is dead and inert. It therefore undergoes no further change. In this respect calcareous differs from fatty

degeneration, in which subsequent changes invariably take place—either softening, caseation, or calcification. It differs also in its effect upon the tissue; for, unlike fatty metamorphosis, it does not cause annihilation of the tissue-elements. The tissue is simply impregnated with calcareous matters, which have no other effect upon it than to render it inert; its vitality is destroyed, but its structure—in so far as the calcification is concerned—remains unaltered.

Calcification must thus be looked upon in many cases as a salutary lesion, the impregnation with calcareous matters preventing subsequent changes in the part. This is especially the case when it occurs in caseous *tubercular foci*, as it imprisons the cause of the disease. It is doubtful whether calcification of a *tumour* is of any benefit to the patient, for the infiltration is probably limited to the dead or dying parts of the growth and does not hinder its spread. On the other hand, when it affects the arterial system, calcification may be attended with the most deleterious consequences, as will be seen in the following section.

Calcification of Arteries.

Calcification of arteries, like fatty degeneration, may be *primary* or *secondary*. As a **secondary** change it occurs in **atheroma** and forms one of its final stages. In this form it is constantly met with in the aorta and its branches, and in many other situations.

Primary calcification is essentially a senile change, a result of that impairment of nutrition which appears and increases as life advances, but which appears earlier and increases more rapidly in some than in others. The change is more or less general. It is associated with atrophy of the arterial tissues, and in some cases with fatty degeneration. It usually occurs in vessels of medium size, the arteries of the upper and lower extremities and of the brain being those most commonly affected. Its most common seat is the middle coat, where it commences in the muscular-fibre cells. The calcareous particles, deposited from the vasa vasorum, make their appearance at first around and within the nucleus, and gradually increase until they fill the cell, which becomes converted into a small calcareous flake. The process may go on until the muscular coat is completely calcified; or it may be limited to isolated portions of the coat, giving rise to numerous irregularly distributed calcareous rings and plates. These are best seen in vessels clarified in spirit and turpentine. From the muscular

it may extend to the external and internal coats, until ultimately the vessel becomes calcified throughout.

The vessel thus calcified loses its elasticity and contractility; its lumen is diminished, and it is transformed into a hard, rigid, brittle tube, or "pipe-stem artery." Such an artery is strengthened against dilatation, but is predisposed to rupture: in amputations great difficulty may be found in securing such vessels, as ligatures cut through them at once. The nutrition of parts supplied by them is more or less impaired, and tubular calcification of the arteries of the lower limb therefore predisposes to "senile gangrene" (p. 24), inasmuch as it renders the vessels less able to adapt themselves to the varying requirements of the circulation.

CHAPTER VIII.

PIGMENTARY DEGENERATION.

Pigmentary Degeneration, or Pigmentation, consists in an abnormal formation of pigment in the tissues.

Normally, many pigments occur in the body, and probably all are the results of cell-action upon hæmoglobin. Some of them pass out in the fæces and urine; others are deposited as normal constituents in cells, the best examples being the cells of the rete Malpighii (especially in the negro) and those of the pigment layer of the retina. But pigment is not limited to epithelial cells; it exists in the cells of the choroid and iris, of the sclerotic (lamina fusca), and of the pia mater. Muscle also is pigmented, and yellow or brown granules may sometimes be seen in the heart.

Pathological pigmentations may be arranged under four headings, according as the pigment is derived: (1) directly from *hæmoglobin;* (2) from the blood by *cell-action;* (3) from *bile;* (4) From *extraneous substances* introduced into the body.

1. **Hæmatic Pigments,** or those derived directly from hæmoglobin, are the commonest. Red corpuscles break up, and their hæmoglobin becomes dissolved. This may occur either within the vessels (malaria, septicæmia), which is uncommon, or after escape of the corpuscles into the tissues. The latter is due either to wounds or rupture of the vessels, or to congestion or inflammation without any breach in

the vessel-wall. Such causes of pigmentation are common; witness the frequency of bruises and apoplexies, of congestions from varicose veins, portal obstruction, and cardiac incompetence, and of stains after various inflammatory lesions.

All are familiar with the changes in colour which occur after a bruise—first purple, then green, and finally yellow. These colour-changes are due to corresponding tissue-changes which follow the infiltration of the skin by the extravasated blood. Briefly, these changes are as follows. 1. Some of the fluid and cells are absorbed at once by the lymphatics. 2. The hæmoglobin is dissolved out of many red cells, and the stromata disappear—no doubt after fatty degeneration. A red fluid is thus formed which infiltrates the tissues, and stains them yellow or brownish-red: the cells are coloured more deeply than the intercellular substance, or than the membranous or fibrous structures. The colour-changes on the surface are owing to changes in this dissolved hæmoglobin, which is soon decomposed into hæmatin and an albuminoid body; part of the hæmatin is reabsorbed and appears in the urine as urobilin, the rest undergoes a change and is deposited as granular or crystalline hæmatoidin. 3. Many corpuscles simply shrivel into brownish granular masses of pigment—said to occur chiefly in "hæmatomata," or tumour-like collections of blood. 4. Many—according to some, most—red corpuscles, or the pigment masses resulting from them, are taken up by leucocytes, which wander in large numbers into the extravasation, and are converted in them into hæmatoidin. The pigment thus formed may be deposited on the death of the cell, or it may be carried by the cell into the lymphatics when it will probably be arrested in the nearest lymphatic glands, the lymph-paths of which will be found beautifully marked out by pigment; or it may pass through into the circulation and give rise to pigment-emboli of various organs.

Hæmatoidin appears to be closely allied to—according to some, identical with—the colouring matter of the bile, bilirubin, which is also a derivative of hæmoglobin. It exhibits similar reactions when treated with concentrated mineral acids, displaying the same variations of green, blue, rose, and yellow colours. It is insoluble in water, alcohol, ether, acetic acid, and in dilute mineral acids and alkalies; it is soluble in concentrated acids, and in the caustic alkalies, giving, in the latter case, a red colour. It does not contain iron. Mixed with hæmatoidin, and very closely resembling it, is a pigment containing iron. This has been named "hæmosiderin."

These final stages of extravasated blood occur in two forms—granular and crystalline. Both are of a very permanent nature, and may remain unaltered for years.

The granules of hæmatoidin vary in size from the smallest particles to masses as large as a red blood-corpuscle. The larger are commonly irregular in shape, sharply defined, and more or less glistening. Their colour varies from yellowish red to brown or black; the older they are the darker they become. The smaller granules are usually dull and opaque.

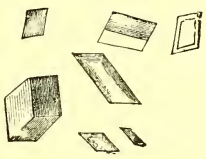


FIG. 33. — *Hæmatoidin Crystals.* (Virchow.)

The crystals of hæmatoidin are opaque rhombic prisms, usually of a beautiful yellowish-red or ruby-red colour, sometimes approaching to brown or black. They may also occur as little plates and fine needles, but these are less common forms (Fig. 33). They are in most cases so small that considerable care is required to recognise their crystalline nature under the microscope, and they may easily be overlooked as merely irregular granular masses. In some cases, however, they attain a larger size. They are more or less transparent, and present a shining, strongly refracting surface.

Intensely black pigment, granular or crystalline, has been called *melanin*. This term, as at present employed, includes several different pigments; some containing iron and some free from it.

Whether hæmoglobin is converted into granular or crystalline hæmatoidin appears partly to depend upon the tissue in which it is situated, crystals being exceedingly common in some situations, *e.g.*, the brain and ovaries; whereas in others, *e.g.*, mucous membranes, only granules are met with.

According to Kunkel, some of the pigment left by hæmoglobin is pure hydrated peroxide of iron.

As to the ultimate fate of extravasations :—

1. Absorption may be, and in vascular parts often is, to the naked eye, complete; but crystals or granules of hæmatoidin may not infrequently be found by the microscope. 2. A yellowish, brownish, or blackish scar, from granular or crystalline pigment, may mark the site of the destruction of tissue by hæmorrhage. 3. A collection of prune-juice or chocolate coloured fluid may long remain surrounded by a capsule of inflammatory tissue, often lined by layers of clot, more or less decolorised and organised (hæmatoma); the fluid contains pigment and fat granules and cholesterin crystals. 4. The fluid may be absorbed

and the clot become completely decolorised and organised—a good example of which is seen in the so-called "membranous pachymeningitis." The process can frequently be watched in aseptic wounds. 5. A cyst, with more or less pigmented walls, containing clear fluid, may be left—especially in the brain.

Pigmentation is a very common form of degeneration, but, fortunately, one of little importance. The presence of pigment in or between the cells of a tissue can have little effect on the elements or their functions: any disturbance of these must be attributed rather to the conditions upon which the formation of the pigment depends. As evidence of antecedent conditions (hæmorrhage, congestion or inflammation), the presence of hæmatoidin may sometimes stand alone—*e.g.*, after cerebral hæmorrhage from capillaries, crystals of hæmatoidin may alone remain; again, slate-grey discoloration of the intestinal mucosa points either to chronic catarrh or portal congestion, and that of the vesical mucosa to chronic catarrh. Slate-grey discoloration, seen post-mortem on solid abdominal viscera, and depending on the action of sulphuretted hydrogen (from decomposition) upon the iron in hæmoglobin must not be mistaken for true pigmentation.

2. **Pigment derived from the blood by cell action.**—The chief examples of this change are melanotic warts, nævi, sarcomata, and carcinomata. The pigment lies in the cells more often than between them, is granular, and varies from yellow to black in colour; it probably contains iron. It differs spectroscopically from all known blood-pigments, and is often included among the melanins.



FIG. 34.—*Cells containing Pigment.* From a melanotic sarcoma of the liver. × 350.

The bronzing of the skin in Addison's disease is not satisfactorily explained. Irritation of the abdominal sympathetic is believed to cause increased pigmentation.

Variations in the normal pigmentation of the skin occur during pregnancy and with various uterine troubles, in leucoderma and melanoderma; but no certain explanation of these, or of blanching of the hair from neuralgia or fright, can be offered.

3. **Pigmentation from Bile.**—The only well-established cause of this variety is obstruction of the hepatic or of the common bile duct. This is most frequently due to swelling of the walls from catarrhal inflammation, to blocking of the lumen by gall-stones, or to the pres-

sure of a growth outside the duct. The bile secreted behind the obstruction is absorbed by the veins and lymphatics, and distributed throughout the body. It appears first in the urine, soon after in the conjunctivæ and skin, and may ultimately stain all the tissues yellow or greenish-yellow. The staining of the skin is known as *jaundice* or *icterus*, and persists some time after the bile has ceased to circulate in the blood. When the seat of obstruction is in the small bile-ducts, as in cirrhosis, the change may be limited to small areas of the liver.

The pigmentation is due to diffuse staining; but granules and even crystals of bilirubin are occasionally found, especially in *icterus neonatorum.*

With regard to the slight jaundice that occurs in septicæmia, the malignant forms of acute infective fevers, and some other diseases, no marked obstruction can be demonstrated in the ducts, and the exact cause is doubtful. It is probable that both increased consistence of the bile, and diminished pressure in the blood-vessels may each cause the tension in the ducts to exceed that in the blood-vessels, or at any rate, in the lymphatics, and thus induce a slight absorption of bile into the vessels, and a consequent mild degree of jaundice. This is the most probable explanation of many of the doubtful cases

4. **Pigmentation by extraneous substances.** — Examples of this form of pigmentation occur in the lungs, the skin, the lymphatic glands, and the mucous membranes. The substances accredited with its production are carbon, silver, lead, arsenic, and such pigments as may be used artificially; to these may be added, in rare instances, mercury, and picric acid.

The inhalation of fine particles of **carbon** and other substances produces pigmentation of the lungs and bronchial glands. This is of considerable importance and will be described in the next section.

The prolonged administration of salts of **silver** leads to the development in the skin and adjacent mucous membranes of a peculiar brownish-grey colour. That portion of the metal which finds its way to these parts is, owing most probably to the action of the light, deposited as an oxide. This condition is known as *argyriasis.* It is permanent.

The presence of **lead** in the tissues is often demonstrated by the occurrence of a narrow, well-defined black line *in* the gums where they are in contact with the teeth. It is due to the action of the sulphuretted hydrogen, given off by the decomposing matter which collects between the mucous membrane and the teeth, upon the lead in the adjacent

tissue. The "lead-line" is, therefore, usually broken, and, in those whose teeth are kept thoroughly clean, often absent, even though other symptoms of lead poisoning may be present. Pigmentation of the mucous membrane of the large intestine has been found associated with the presence of considerable quantities of lead and of **mercury** respectively in that part of the alimentary tract.

In **tattooing**, artificial pigments are placed in the deeper layers of the skin. Most of the pigment remains in its original position. Of the remainder, some is devoured by wandering leucocytes, and some is washed on into the lymphatics and filtered out by the glands where it is retained.

Dead tissues in process of separation are frequently discoloured—black, greenish-black, or slate-grey—by the action of sulphuretted hydrogen; and *atrophied organs,* in which the pigment is, as it were, concentrated, often appear darker than normal. Neither of these, however, is an instance of true pigmentation.

Pigmentation of the Lungs.

In no organs is pigment met with so frequently and in such large quantity as in the lungs, and much discussion has arisen as to its nature and origin. Its amount gradually increases with advancing age—the lungs of infants being free from it, whereas those of adults invariably contain considerable quantities.

This pigmentation of the lungs is due principally to the presence of carbon, and not of hæmatoidin. The carbon—derived from incomplete combustion of wood, coal, and other substances, and always present in varying quantities in the atmosphere—is inhaled, and the minute particles pass into the finest bronchi. Many are taken up by mucus-corpuscles, and may be seen as small black granules in the cells of the greyish-black sputum frequently expectorated in the early morning Much of the carbon is thus eliminated by expectoration; but many particles pass into the air-vesicles, and here, their removal by this means being less readily effected, they gradually penetrate into the alveolar walls and interlobular tissue. Most of the pulmonary pigment is found in these situations, either within the connective-tissue cells or free among the fibres (Fig. 35).

According to Tyndall exhaled complemental air is free from particles. The carbon-particles can be carried by the air only so far as it is tidal or complemental. Any cilia would work against the descent of the

particle and its carrier cell. The difficulty with which septic organisms gain access to the minute ramifications of the air passages is shown by the rarity with which empyemata from perforation of the lung putrefy, and by the ready disappearance of putrefaction in offensive sputum when intra-laryngeal injections are employed.

The means by which the particles of carbon can penetrate the walls of the air-vesicles, and make their way into the inter-alveolar tissue, has been explained by Klein. The branched connective-tissue cells



FIG. 35.—*Pigmentation of the Lung.* From a woman, æt. sixty-five, with slight emphysema. Showing the situation of the pigment in the thickened alveolar walls, and around the blood-vessel *v*. The walls of the latter are also thickened and its lumen diminished. × 75.

of the alveolar walls send a process, or a greater or less portion of their body, between the epithelial cells of the alveolus into the alveolar cavity. As these connective-tissue cells lie in the serous canals which constitute the commencement of the perivascular lymphatics, it is easy to understand how these openings in the alveolar walls (pseudo-stomata) may become sufficiently distended to allow cells and other substances to pass through from the alveolar cavity into the inter-alveolar tissue. When once the carbon has made its way into the inter-lobular tissue, some of it is taken up by the fixed cells in this situation, whilst that, which is not thus detained, passes on to the lymphatics, and is deposited in the bronchial lymphatic glands, where the black particles are also visible. The wandering leucocytes, probably convey particles from the lumen into the mucous membrane of the bronchi.

Closely allied to this physiological pigmentation of the lung from

the inhalation of carbon, are those morbid conditions which result from the inhalation of particles of coal, stone, iron, and other substances —of which the lungs of miners, stonemasons, and grinders afford frequent examples. Here also minute particles enter the bronchi, penetrate the walls of the alveoli, and are deposited principally in the interstitial tissue. In the case of miners—in which this is most common—the particles of coal enter the lungs in such large quantities as to give to them an almost uniform dark black colour (*anthracosis*). In stonemasons, grinders, and others, the lungs also become deeply pigmented (*silicosis*), although to a less extent than those of miners.

The black colour of the lungs in these cases, however, is not entirely due to the presence of the inhaled substances, but partly to that of hæmatoidin. The inhaled and irritating particles set up inflammatory changes in the bronchi and pulmonary-tissue, causing chronic bronchitis, chronic catarrhal pneumonia, and a large increase in the fibrous tissue of the lungs, which thus become consolidated, tough, and fibrous. In the most severe forms, ulceration, starting from the bronchi, produces cavities ("Colliers'" and "Knife-grinders' Phthisis"). Owing to these structural changes there is a considerable escape of red corpuscles from rupture of capillaries or inflammatory exudation, and hence a large formation of pigment, to which much of the dark colour of these lungs must undoubtedly be ascribed. The lungs of stonemasons and grinders are, like those of miners, deeply pigmented, though to a less degree; but the black colour in the former cases cannot be entirely accounted for on the supposition that it is due to the presence of inhaled particles. Carbon particles are black, angular and very variable in size and shape. They are unaffected by strong acids and alkalies. Pigment derived from the blood is generally brownish and granular.

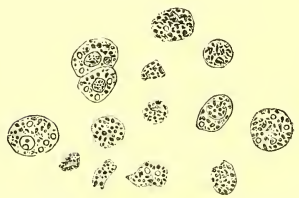


FIG. 36. — *Cells from the Sputum of Acute Bronchitis.* Showing the minute granules of pigment within the cells. Some of the cells also contain a few fatty molecules. × 400.

Pigmentation of the lungs from the presence of hæmatoidin occurs as the result of many other morbid conditions, many diseases of these organs being attended by the formation of pigment. In chronic phthisis, pigmentation occurs, partly as the result of the inflammatory process, and partly from the obstruction of the vessels caused by the new tissue: lines of pigment are constantly seen surrounding the nodules of consolida-

tion. In acute croupous pneumonia, the blood which is extravasated into the air-vesicles, and which in the early stages gives to the expectoration a rusty or prune-juice colour, subsequently becomes converted into pigment, and the sputum becomes of a greyish-black ; the pigment granules being visible in the newly-formed cells. The cells met with in the sputum of bronchitis also contain granules of pigment (Fig. 36) ; and pigmentation plays an important part in the condition of the lungs known as brown induration.

Pigment in the lung usually occurs as black irregular granules ; it is rarely met with in a crystalline form. In all cases in which it is found in any quantity in the lung it is found in the bronchial glands also. It is taken up by the lymphatics, and, like the inhaled carbon, becomes arrested in its passage through these glands, where it remains permanently.

CHAPTER IX.

NUTRITION INCREASED.—HYPERTROPHY.

The morbid processes thus far described have been attended either by arrest or by impairment of nutrition ; there remain to be considered those in which the nutrition is so changed that formation exceeds waste and growth results. They include **hypertrophy**, **regeneration** and **tumour-formation.**

Normal growth depends upon : (1) the inherited tendency of the cells to grow ; (2) the supply of food ; and (3) the amount of waste. In all abnormal overgrowth one or more of these factors are at fault. There is, however, a marked distinction between hypertrophy and regeneration on the one hand, and tumour-formation on the other. In the former the new tissue is an exact reproduction of the original, and has the same function ; in the latter, the structure of the new tissue is not an *exact* reproduction of the old, and the arrangement of its elements is still more distinctive, while no tumour possesses any known function.

Hypertrophy.

Hypertrophy may be defined as an "increase in the size, weight, and functional activity of a part beyond the limit of health, due to an

orderly enlargement or multiplication of all its normal constituents." From this definition it will be seen that the *nature* of the process is strictly physiological; in *extent* only it is pathological. External form and minute structure alike exhibit a single change—that of size. The weight of an hypertrophied organ, however, gives the most reliable indication of the extent of the change. Strictly proportional to the increase in size and weight is that in functional activity.

The terms "false hypertrophy" and "pseudo-hypertrophy" are used to indicate that the increase in size, while presenting a superficial resemblance to hypertrophy, is due either to the unequal overgrowth of the tissue-elements, or to the growth of only one of them—often at the expense of the rest; and that there is no increase in functional activity. Thus pseudo-hypertrophic muscular paralysis is characterised by a marked enlargement of certain muscles, due to an increase in their connective-tissue elements, and accompanied by atrophy of the muscular tissue, and diminished functional activity.

Hypertrophy is said to be "simple" when it is due to an increase in the size of the elements of the affected part; "numerical," when to increase in their number. The latter is also called hyperplasia. These terms are of little practical value; for hypertrophy is in nearly all cases believed to be numerical; and in most cases it is simple as well. In the great example of physiological hypertrophy—the gravid uterus—some of the muscular fibres may be ten times their normal size.

ÆTIOLOGY.—In many cases we cannot say how far a given instance of hypertrophy is due to excessive vital energy of the cells of the part, to the setting aside for its embryonic rudiment of too large a number of cells, to diminution of the resistance to growth, to an ampler food-supply, or to diminished waste.

In a large number of cases hypertrophy seems to occur as a response to a demand which has arisen for increased work. Thus a difficulty arises in the circulation. It may be due to a narrowing in the arterioles, or to obstruction at one of the orifices of the heart, or to some interference with the movements of the heart-walls themselves, such as may be caused by the permanent adhesion of the visceral and parietal surfaces of the pericardium. Under the altered conditions the normal blood-flow can only be maintained by increased functional activity on the part of the heart. Now it generally happens that in proportion as the difficulty gradually makes itself felt, so the part or parts of the heart upon which the extra work required falls, gradually

hypertrophy: thus the increased demand is permanently provided for. At the same time the supply of blood through the coronaries is also increased. It would seem, indeed, that this is the connecting link between the increased functional activity and the production of the hypertrophy; for if, through disease of the coronaries or other cause, an increase in the blood supply to the heart cannot be effected, the requisite hypertrophy does not occur. When hypertrophy arises in this way it is termed "compensatory."

The power of an organ thus to hypertrophy is by no means unlimited. One source of limitation is very clear: this is in the blood-supply. If, in any way, the quality of the blood deteriorates, or the coronary vessels become rigid or partly obstructed, not only is increased growth an impossibility, but, as has already been said, fatty degeneration will inevitably ensue (p. 49). The other chief source of limitation lies in the "growing capacity" of the cells. When the original disease is of a progressive character, or when its ravages are increased by the help of allied diseases, it is clear that there must come a time when, even though the coronary circulation be apparently adequate, the inherited capabilities of the cells will fail, and growth consequently cease. We know very little concerning this inherited growing capacity; but it is a very important item. Probably no increase of the blood-supply could save a thymus gland from atrophy or increase the number of adult ganglion cells.

When muscle contracts frequently against an increased load, it hypertrophies—as is seen in training—unless the load is *too* heavy, when atrophy may result. Frequent contraction alone is insufficient, for the muscles of hands used actively but not forcibly do not enlarge, nor is frequent micturition in pyelitis followed by thickening of the muscular walls of the bladder. But insert an obstruction in the urinary passages, which the bladder can, by more powerful contraction overcome, and hypertrophy begins. Other examples of these *compensatory* hypertrophies may be seen in the walls of the intestine just above a permanent stricture or in those of a vein in aneurysmal varix, or of any vessel through which an abnormal quantity of blood is forced.

When an organ is removed, or prevented from fulfilling its ordinary function, other organs which take on its work hypertrophy, receiving the blood which should have supplied the diseased organ as well as their own. This is best seen in the kidney; rarely in the testis and lung. Removal of one submaxillary gland is not necessarily followed by hyper-

trophy of other salivary glands ; this would occur only from more frequent stimulation of their secretory nerves, which probably produces the large submaxillary glands seen in epithelioma of the tongue. But the kidneys are under nerve-control in a different way ; they seem to be excited to secrete by the presence in the blood of material suitable for their secretion, and hypertrophy naturally results from continued greatly increased supply of blood containing excess of urea, and other products of tissue metabolism. Enlargement of lymphatic glands has been noted after removal of the spleen. Increased weight thrown on a bone causes thickening of it—*e.g.*, of the fibula in ununited fracture of the tibia.

Repeated hyperæmia from hard use and slight injuries is followed by thickening of the epithelium, as in a labourer's hand. Under similar conditions, a corn may arise. Increased blood-supply to a limb may cause lengthening of a bone, if the epiphysis be ununited, as has been seen in large ulcers, caries, necrosis, and other conditions. The soft parts increase secondarily.

The hypertrophied spleen of intermittent fever, and the thyroid in endemic goître (Klebs), are due to active hyperæmia, perhaps excited by the presence of organisms. Exophthalmic goître has been attributed to vaso-motor paralysis from disease of the sympathetic ganglia, but it is very doubtful if it could result from such a lesion.

Diminished waste is, apparently, not a common cause of hypertrophy. An example often quoted is the sub-involuted uterus, the bulk of which is made up of hypertrophied muscle, and connective-tissue with thick-walled vessels, but it is doubtful whether chronic inflammation is not largely responsible in these cases. Uncut hair and nails, and, in the case of many animals, unopposed teeth, grow till their vessels supply only nutriment enough to maintain them in their finally attained condition. The sclerosis of bone produced by small doses of phosphorus, the increase in size and strength of animals treated with small doses of arsenic, and the invigorating effect of this drug upon Styrian mountaineers, may perhaps be explained by diminished waste.

The **removal of resistances to growth** is difficult to ascertain. It seems to be a factor in the production of such deformities as "knock-knee" (*genu valgum*) : here excessive pressure is thrown on the outer articular surfaces of the femur and tibia, whilst the weight borne by the inner surfaces is less than normal, and they, consequently, grow excessively. Many *scleroses* or hypertrophies of connective-tissue follow

upon atrophy of the essential elements of the organ: the natural resistance between the two tissues has been removed (see p. 123).

There remain certain cases in which the ætiology is even more doubtful than in the above. First, cases of *true "giant-growth"*—increase in length, rather than in breadth, being implied; hypertrophy of the whole body (giants); of half the body; of whole limbs or of parts of them, as fingers and toes. Such parts are, on dissection, normal, except in size. Secondly, cases of *false giant-growth* in which the connective-tissue alone is increased, the part being often misshapen; lymphatics are often dilated, and the blood-vessels may be nævoid. Examples are met with especially in the lip (*makrocheilia*), tongue (*makroglossia*), and lower extremity. Hypertrophy of connective tissues and surface epithelium may result from an excessive, though slow and impure, supply of blood. In some of the above, which are congenital or appear soon after birth, there may be **excessive vital energy** or **too large a number of the cells** forming the rudiment of the part or tissue.

Nothing is known of the causation of senile hypertrophy of the prostate; nor of the enormous, but rare, enlargement of the female breast which may occur at puberty.

Hypertrophy of the Heart.

Hypertrophy of the heart has been already referred to, but is of sufficient importance to merit a more detailed account.

The whole heart may be uniformly affected or the enlargement may be mainly confined to one of the two ventricles.

Uniform hypertrophy of the whole organ is a common result of adherent pericardium. By this change the sliding action of the heart is interfered with, and the work thrown upon its muscular walls proportionately increased. A heart thus enlarged may weigh from twelve to thirty ounces—even after the parietal layer of the pericardium has been dissected off. The normal shape of the heart is preserved, but its general dimensions—both external and internal—and the thickness of its walls are alike increased.

Hypertrophy of the left ventricle follows any changes that give rise to obstruction at the aortic orifice, or permit regurgitation from the aorta. It also follows obstruction in the arterioles such as occurs in some forms of chronic Bright's disease. The weight of the organ frequently exceeds twenty ounces. In shape it is elongated; the septum, and therefore the left coronary artery, is displaced to the

right of its usual position on the anterior surface. On examining a vertical section the apex is seen to be formed entirely out of the wall

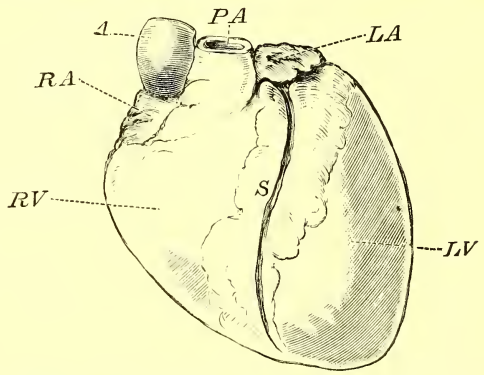


FIG. 37.—*Hypertrophy of Left Ventricle* (front view). Heart is elongated. Septum occupies middle of anterior surface. From a case of granular kidney. From a specimen in Charing Cross Hospital Museum.

of the left ventricle, and the walls of this cavity are themselves thickened (Fig. 39).

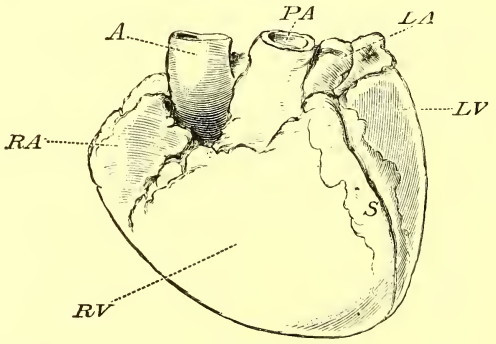


FIG. 38.—*Hypertrophy of Right Ventricle* (front view). Heart is quadrilateral and septum is displaced to the left. Right auricle is dilated. From a case of chronic bronchitis and emphysema. From a specimen in Charing Cross Hospital Museum.

Hypertrophy of the right ventricle follows corresponding changes in the mitral orifice, and regurgitation from the left ventricle. It may also be due to obstruction to the flow of blood through the lungs as in emphysema (p. 38). In this case the heart is quadrilateral, and

its anterior surface consists, almost entirely, of the wall of the right ventricle. On section both ventricles are found to take about an equal share in the formation of the apex of the organ, while the usual difference

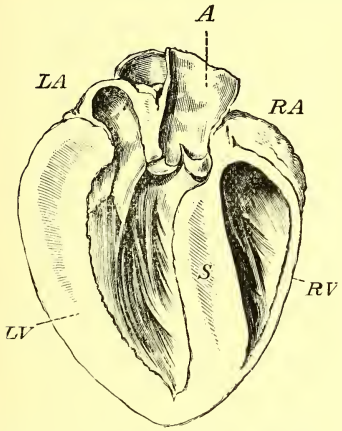


FIG. 39.—*Anterior half of Heart* (Fig. 37) *seen from behind.* Left Ventricle forms the whole of apex. Wall of *LV* : wall of *RV* :: 10 : 2 (normal proportion 5 : 2).

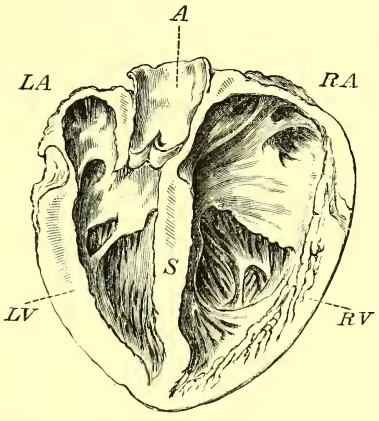


FIG. 40.—*Anterior half of Heart* (Fig. 38) *seen from behind.* Right Ventricle is seen to take greater share in formation of apex than Left Ventricle does. Wall of *RV* is much thickened, but not so thick as that of left. Tricuspid orifice and *RA* are dilated.

between the thickness of the walls is much diminished. Except in cases of congenital disease, the thickness of the right ventricle never reaches that of the left. These distinctions are well shown in the accompanying illustrations.

CHAPTER X.

REGENERATIVE PROCESSES.

DESTRUCTION of tissue-elements has frequently been described in earlier chapters as the result of injuries and various degenerative and inflammatory processes. We must now briefly state how such losses are repaired. It has already been said (p. 12) that the cells of one embryonic layer always produce tissues originally developed from the same layer; and it is apparently true also that true regeneration of a tissue occurs only from cells of that tissue—muscle from muscle,

epithelium from epithelium. Any form of connective-tissue may, however, give rise to any other form—areolar tissue, bone, cartilage, &c. With regard to the origin of these tissues from leucocytes—if this ever happen—the latter must, when we consider their sources, be considered as connective-tissue corpuscles.

The regenerative processes which may go on in adult mesoblastic tissues, are still imperfectly known. Their reproductive energy has been supposed to be limited to molecular repair. Nevertheless, it is certain that the cells of most adult tissues retain the power of multiplication. That this is not manifest under normal conditions, is possibly because the blood-supply the tissues receive is sufficient only to maintain the *status quo*, while the resistances opposing growth, such as pressure within the tissue, are equal to the force with which they tend to multiply. But if the intercellular pressure be loosened by wound or by destruction, absorption of the damaged elements and multiplication of cells round about will begin. Such injuries usually increase the blood-supply.

So far as investigation has yet gone, the nuclear figures, described at p. 11, have been found in each tissue to form the first stage of division of cells.

As no extensive regeneration occurs without the formation of new vessels, we shall first state what is known concerning their production.

Vessels.

The formation of new vessels has been studied chiefly in the tadpole's tail, in sections of healing wounds, and in teased preparations of granulation-tissue. At the end of the second day after the infliction of a wound, and later, solid pointed processes are seen projecting from cells forming the walls of capillaries; they increase in length and join similar processes from other capillaries, or, occasionally, processes of branched connective-tissue corpuscles. At first very fine, the processes gradually widen and become hollow, and thus an anastomosing set of vessels (*intra*-cellular channels) is produced. At this time a few nuclei are seen in their walls, the result of division of the original cell-nuclei, but nitrate of silver does not show the lines of union of individual endothelial cells. These develop subsequently. The process corresponds with that observed in the embryo (with the exception that no red corpuscles form in the cells), and is the same in the healing of wounds, in new growths, and in reproduction of lost parts.

Two much less certain modes of origin of vessels are described. (1) In granulation-tissue, Thiersch states that lymph-streams issuing from the vessels form channels between the loosely connected cells, which ultimately communicate with vessels, and fill with corpuscles. Observations of Birch-Hirschfeld support this view. (2) Spindle-cells in granulation-tissue are said so to arrange themselves as to form canals which communicate with vessels. It is probable that they are really collected round a bud from a vessel (Ziegler).

As in the embryo, the new vessels may increase in size with the demands made upon them, muscular and fibrous coats being formed by cells which apply themselves around the original tube.

Adult vessels may increase greatly in size and thickness, as is seen in the gravid uterus and collateral vessels of a limb in which the main trunk has been tied; such vessels generally become tortuous as well as wider. Increased flow through the vasa vasorum is always present.

Common Connective Tissue.

This is the most frequent seat of new formation of all kinds—hypertrophy, tumour formation, and regeneration. With regard to the latter, it seems most probable that loss of substance is made up by multiplication of the surviving connective-tissue cells. For a time it was thought that adult connective-tissue corpuscles were incapable of growth, and that almost all new fibrous tissue was formed from wandering leucocytes. The difficulty in estimating the part played by each of these elements is extreme. Senftleben's experiments on the cornea prove the regenerative power of connective-tissue cells. Sherrington and Ballance deny leucocytes any fibrous tissue-forming power. Metchnikoff believes that only the large mononuclear leucocytes are capable of such development. The subject is discussed more fully in the chapter on "Inflammation."

Adipose Tissue.

This is merely connective-tissue, of which the cells are infiltrated with fat. Newly formed connective-tissue cells may certainly thus become infiltrated—*e.g.*, in pseudo-hypertrophic, and, to a less extent, in infantile paralysis; but inflammatory tissue as a rule remains free from fat.

Cartilage.

A wound or breach in cartilage is generally repaired in the first instance by scar-tissue. This may be replaced later by hyaline cartilage formed from the perichondrium, and by proliferation of neighbouring cartilage-cells. The matrix is formed, according to Strasser, from the protoplasm of the cells. Often this replacement by cartilage does not occur. In cases of fractured rib-cartilage the fibrous tissue may ossify into a clasp of bone round the broken ends.

Bone.

The regenerative power of bone is considerable. It depends chiefly upon the periosteum, and to a less extent upon the marrow. The process is best illustrated by the repair of a simple fracture.

Repair of a Simple Fracture.—During the first twenty-four hours an examination shows the broken ends of the bone lying in a collection of blood coagulated where it is in contact with the tissues, but fluid round the fracture. The ends of the bone are sharp and jagged, the periosteum is more or less torn and stripped off, and the medulla deeply ecchymosed. The injury to the vessels of the part excites exudation of fluid and of cells: the torn tissues are infiltrated by these cells, so that in three or four days they are found to have lost their earlier appearance, and to have become soft, pink, and gelatinous, as is best seen in the medulla. In fact, they are "granulating" and the granulation-tissue increases in amount until the blood around the fracture has altogether disappeared, and the ends of the bones are embedded in a mass of soft tissue. This tissue is formed from the periosteum, medulla, and any other soft parts that are injured. From the third or fourth day certain large angular cells are seen close to the bone: these play the part of osteoblasts. Here, as elsewhere, the source of the cells of the granulation-tissue, after the effect of the primary injury has subsided, is disputed; some referring their origin to leucocytes, but the majority to the cells of the medulla and periosteum. Possibly both contribute: the effect of irritation (mobility of fragments) in causing free formation of new tissue is urged in favour of a largely leucocytic origin. This soft tissue is found in plenty about the tenth day, when it is difficult to recognise the periosteum, which is swollen and infiltrated with cells like other parts. Next, the granulation-tissue becomes firmer, and at about the fourteenth day the

periosteum can again be seen covering a spindle-shaped swelling, which extends beneath it for some distance up and down the bone. As Billroth says, the ends of the bone are stuck into this spindle-shaped mass as if it were soft sealing-wax; there is a ring outside and a plug in the medulla. This uniting tissue is called the **provisional callus**. In animals it is generally converted into cartilage, but in man direct ossification usually begins in the third week. In man, however, when tolerable rest cannot be maintained, as in fractured ribs and many fractures in children, cartilage may be developed. It is always in greater quantity where the bone is thickly covered by soft parts, and rarely forms a complete ring in man. It is strongly developed in any angle or gap. Where the most perfect rest is obtained, as in fissures of the skull, little or no provisional (or permanent) callus is formed.

Ossification of the provisional callus begins in the angle between the periosteum and the bone, and extends thence beneath the periosteum and along the surface of the bone. The plug in the medulla ossifies a little later. At first the bone is soft and open in structure, and easily picked off the shaft. Its canals are more or less vertical to the surface of the shaft, and continuous with abnormally wide Haversian spaces in the latter. Ossification begins round the vessels passing from the callus to the bone: the cells farthest from the vessels assume the shape of osteoblasts, and become surrounded by or converted into bone. Osteoblasts inside each ring next lay down laminæ of bone until Haversian systems are formed. The callus is now intimately united with the original bone, and holds the ends firmly together. The medullary canal is blocked by bone, and osseous buttresses fill up any angle. This complete ossification of the provisional callus is finished in man between the fourth and eighth weeks, according to the size of the bone.

So far the bony tissue has not been mentioned. The next step is to unite the two ends directly by what is termed **permanent** or **definitive callus**. This begins to form when the provisional callus has fixed the ends of the bones; but preparation for this union begins much earlier. The ends of the bones are to be softened into a tissue which can bridge over the gap, blend the two fragments into one, and finally ossify. A rarefying ostitis begins in all probability immediately after the injury, and results in a round-celled growth, which slowly eats away the walls of the Haversian canals which thus become enlarged. Naturally this is a much slower process than similar infiltration of the

soft parts. So long as the bones are moving on each other, the granulations would have little chance of blending across the gap; but so soon as the fragments are fixed this union occurs, and ossification, running on to sclerosis, follows. It is probably not complete before the fourth month.

The final process in the union of a simple fracture is the rounding off of all prominences, and the absorption of all unnecessary provisional callus. The completion of this may occupy years; but, ultimately, in an accurately set fracture, the medullary canal may be opened up and most of the thickening around the shaft removed. Generally the seat of fracture remains evident, but Billroth says that in some cases it cannot be recognised. The analogy between the repair of bone and the repair of ordinary connective-tissue, as described under healing of wounds, scarcely needs pointing out; ossification of the scar-tissue is the main difference.

Repair of compound fractures is effected by the ossification of granulation-tissue, either directly or after its conversion into fibrous tissue. But suppuration, implying more or less destruction of the new tissue, and often necrosis of soft and hard tissues, greatly delays the process (see "Necrosis of Bone"). Even where compound fractures become simple from the first by union of the wound they are often much longer in healing: the reason is not evident.

Muscle.

A wound in muscle as a rule gapes widely and heals by granulation In some parts, as the tongue, retraction is prevented, and union, by first intention, occurs readily. The protoplasm escapes through the opened sarcolemma, and leucocytes penetrate for some distance between the fibres. Ordinary scar-tissue develops from the granulation-tissue and unites the ends of the muscle. New cells are now produced by the muscle-cells on each side of the scar, and they invade and may eventually replace the cicatricial tissue. Kraske says that new muscle-cells are produced only by multiplication of the nuclei of the old. Each nucleus becomes surrounded by a spindle-shaped mass of protoplasm and divides to form muscle-fibres. In some cases no regeneration is evident.

Regeneration occurs more frequently to repair losses from degeneration, such as that which occurs in acute febrile diseases, especially typhoid. The new cells are believed to spring from small elements

lying between the original muscle-fibres, or by splitting of the old cells from end to end.

Involuntary muscle-cells multiply also by division. There is some doubt as to whether these may not arise from connective-tissue corpuscles.

Nerve-Cells and Nerves.

Nothing is known of a regenerative process among ganglion cells, and many think that none occurs in adult life. An ordinary scar is all that is known to replace destroyed ganglionic-tissue.

When a nerve is cut across, union takes place readily by scar-tissue if the ends are brought together; and, as a rule, function is restored in the course of time, even when a considerable piece (in some cases nearly two inches) has been excised.

After division, myelin escapes up to the nearest nodes of Ranvier, and blood is extravasated between the fibres and in the sheath. Then leucocytes infiltrate the ends for a short distance, rendering them bulbous; the soft parts are similarly infiltrated, and a mass of granulation-tissue soon unites the ends. Later this develops into ordinary scar-tissue.

Beyond the degeneration of a few fibrils, no immediate change occurs in the central end. In the peripheral end, however, changes occur rapidly, and lead to destruction of the nerve. In warm-blooded animals, according to Ranvier, after twenty-four hours, the nuclei in the primitive sheaths are found enlarged, and the sheath is everywhere visible; then protoplasm accumulates round the nuclei, at the nodes and other points, replacing the medullary substance. On the third or fourth day these protoplasmic masses are so large as to completely break up the sheath of Schwann at many points. At the same time the nuclei are seen to have multiplied once or twice. A little later, almost all the degenerated myelin has disappeared, and the axis-cylinders are broken into short segments which may finally suffer the same fate, nothing remaining of the peripheral end of the nerve but the primitive sheaths, distended at intervals by nuclei which are abnormally frequent. Sometimes drops of fat persist. A few fibres do not undergo degeneration. They are thought to have sprung from other undivided nerves lower down, and to be taking a recurrent course in the divided trunk. These fibres degenerate in the central end. These changes are said to begin in the muscle-plates in motor nerves; but they occur practically at the same time throughout the peripheral ends. They are generally complete in fourteen days. The

nerve is now grey and shrunken; its fibrous tissue overgrows, and further wasting and induration follow.

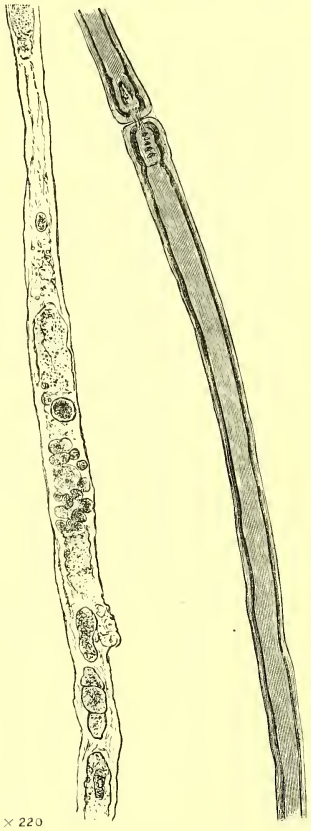


FIG. 41.—*Fibres from the peripheral end of a nerve ten days after section.* Stained with osmic acid. One fibre shows the masses of degenerated myelin; the other is healthy. (From a specimen by Dr. Mott.)

No regenerative changes occur for four or five weeks. Then it is found that the axis-cylinders of the central end are dividing into two bundles (which again divide several times), or into several, and that these small new axis-cylinders are finding their way through the scar-tissue into and between the old primitive sheaths. Growth of the axis-cylinders always begins from a node next above or close to the section, where the sheath of Schwann is bulbous. A cross-section of the peripheral end at about the eighth week shows small medullated and non-medullated nerves, among the old primitive sheaths, full of protoplasm. The course of these new fibres is very irregular, especially through the scar, where they may even loop back. At first non-medullated, they acquire, later, sheaths of Schwann, with nodes of Ranvier, which are at first placed at short intervals, as in young nerves. In the scar, even primitive sheaths are at first wanting; but they ultimately form from the surrounding connective-tissue.

Many months, or even a year, may pass before function is restored, a shorter time being required in sensory than in motor nerves, and it is supposed that during this time the axis-cylinders are slowly finding their way along the nerve. The time varies with the length of nerve beyond the division and with the distance between the ends. The number of axis-cylinders produced in this process is much greater than that of the nerves destroyed. It seems probable, therefore, that many atrophy; but their further history is not known

Cases occur in which restoration of sensation takes place within a few days of the division of a nerve. The probable explanation is that communicating nerves take on the function of the divided one; but Ross and others think that, if the ends are kept in contact, "immediate" union of the axis-cylinders may occur.

When union does not occur, and after removal of the peripheral part, the proximal end becomes bulbous (p. 132).

Epithelium.

Epithelium is always derived from pre-existing epithelium, by simple division of the cells. This is shown by the fact, that it always spreads in from the edge of an ulcer, unless islets of the rete have been left undestroyed in the midst of the granulation-tissue.

The epithelium of the skin and mucous membranes, and of many glands, is being destroyed and replaced throughout life—sometimes very rapidly, as in catarrhs of mucous membranes and of the kidney (acute nephritis).

But if all the cells of an acinus or tubule of a gland be destroyed, there is probably no reproduction of epithelium. A wound of a gland, with or without loss of substance, heals by scar-tissue, which is permanent. According to von Meister, regeneration of liver cells can take place in the dog, cat and rabbit. The matter, however, needs further investigation. The more highly specialised the function the less likely is the tissue performing it to be capable of regeneration.

Regeneration of nails and hair is frequent.

Healing of Wounds.

The union of most wounds and the repair of losses of substance are effected primarily by the formation of more or less scar-tissue—*i.e.*, by the development of new vessels and new connective-tissue. Subsequently more or less regeneration of the injured tissues may take place in the modes above described. Several modes of healing are described, but they are fundamentally the same. They are—(1) Immediate union; (2) Union by first intention; (3) Healing by second intention or by granulation; (4) Healing under a scab; (5) Union of two granulating surfaces.

Immediate Union.—Described by Macartney in 1838, the occurrence of the process has been confirmed by Paget and Thiersch. The

latter states that it occurred in wounds inflicted on the tongues of animals. The union is said to be effected by a blending of the practically unchanged surfaces of the wound, no lymph intervening as a bond. It is complete in twenty-four hours, and no scar results. Most pathologists deny that such a process ever occurs. They believe that lymph, possibly only in microscopic quantity, invariably forms the first bond of union. With them *union by first intention* is the speediest mode of healing possible.

Union by First Intention.—This generally occurs in well-treated incised wounds. It is prevented if the surfaces are not accurately brought together, but left gaping superficially, or separated in their deeper parts by foreign bodies, blood, or fluid exudation in any quantity. It is also prevented by movement of the surfaces on each other; by sloughing of the surfaces; or by irritation of any kind which excites inflammation going beyond the fibrinous stage. When these conditions are avoided by careful arrest of hæmorrhage, cleansing, drainage, apposition, provision for rest, and prevention of septic and infective inflammations, the following changes take place. The capillaries become thrombosed up to the nearest collateral vessel. If any arteries or veins have been tied or torsioned, the changes described in Chapter xviii. set in. An injury inflicted by a knife is severe, strictly localised, and of short duration. It excites free exudation of fluid and corpuscles. At first there are many red corpuscles in the exudation, but they rapidly diminish, and the fluid becomes clear and deep yellow. If this exudation is small in quantity, it can escape between the edges of the wound, but if large, channels should be purposely provided. The fibrin contained in the exudation coagulates on the opposed surfaces, binding them together; it contains a variable proportion of leucocytes.



FIG. 42.—*Union by First Intention.* See text (p. 111).

It is this "lymph" which forms the "glaze" on wounds left open. The exudation diminishes greatly as the effect of the injury passes off. Microscopic examination, after 24–36 hours, shows the edges of the wound separated by a narrow band of small round cells; the tissues close to the incision are swollen and hazy, and more or less infiltrated with leucocytes. New vessels develop after the second day, and shoot across from side to side, converting the lymph into granulation-tissue. This then goes on to the development of scar-tissue. The number of leucocytes about the wound varies with the amount and duration of the irritation; in some cases it is quite difficult to make out what holds the edges together. Thus in a herniotomy wound examined on the fourth day (Fig. 42), the line of incision was recognised almost solely by the fact that the fat on one side was adherent to the deeper layer of the cutis on the other; the two seemed to be in actual contact, and there was hardly any round-celled infiltration. The part taken by the tissue-elements in scar-formation is discussed in Chapter xx. The older a scar is, the more closely does it resemble the normal tissue.

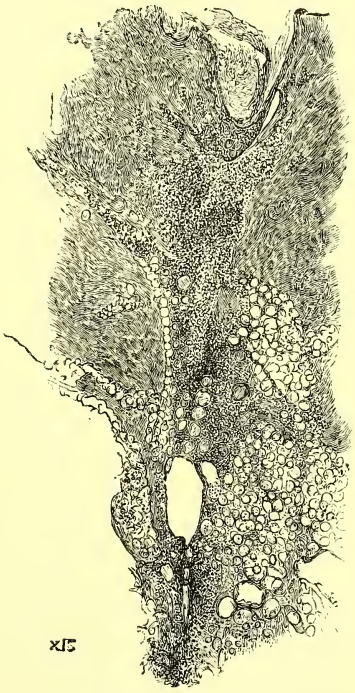


Fig. 43.—*Union of two Granulating surfaces from a breast-wound.* The uniting material is in much greater amount than in Fig. 42. See p. 112.

Union by Granulation. — When a wound cannot be brought together, or when union by first intention is prevented, this form will occur. Until union takes place a raw surface is necessarily exposed to some irritation. This, some think, keeps up a constant exudation of fluid and leucocytes from the new vessels, just as the original injury excited such exudation from the vessels of the normal tissue, and the leucocytes embedded in a little intercellular substance become vascularised into granulation-tissue. The majority of pathologists, however, believe that after the primary severe irritation has subsided,

granulation-tissue is produced by multiplication of the neighbouring connective-tissue corpuscles. However formed, the tissue increases in amount until the wound is filled up to the level of the surface, when the granulations skin over, as described in Chapter xx. A granulating wound, under the old-fashioned dressings, suppurated more or less freely; but one treated antiseptically, and, therefore, protected from irritation by the antiseptic employed, discharges a serous fluid. A section through granulation-tissue shows on the surface a layer of small round cells with bi- or tri-partite nuclei, embedded in a substance which is actually fluid superficially—this layer is breaking down into pus. Deeper down are found fibro-blasts, and, deeper still, scar-tissue in all stages of formation. The thickness of the surface-layer, and the amount of pus formed, vary with the irritation to which the tissue is subjected. In some cases destruction equals or exceeds growth of granulations. Here, again, therefore, treatment should be directed to the avoidance of all unnecessary irritation.

Healing under a Scab.—In this form the exudation is small in amount, and dries into a scab. It is not common in Man except in superficial abrasions. Formation of granulation- and scar-tissue occur beneath it, as also does the inward growth of epithelium. When "skinning over" is complete, the scab drops off. The dry scab is but slightly irritant in itself, and it does not putrefy. When ulceration spreads beneath a scab, some infective agency is probably the cause. The process of scab formation is sometimes imitated by closing wounds, often leading to cavities, with collodion; or by allowing blood or tincture of benzoin on lint to dry and occlude the opening. Such treatment is, however, dangerous; for if septic or infective organisms have entered and excite inflammation, the absence of drainage will be most prejudicial.

Union of Two Granulating Surfaces.—When two surfaces have granulated as above described, they may be brought together; and frequently the two surfaces will blend, thus saving the time which would be required for filling up from below. Free suppuration and imperfect drainage will prevent such union. This is the way in which abscesses should heal when their walls are allowed to fall together by evacuation of the pus (Fig. 43).

Transplantation of Tissues.

Even before John Hunter's success in transplanting a cock's spur into its comb, it was believed that pieces of the body, like the tip of the nose or finger, might re-unite if fixed in position soon after complete separation from the body. But accurate knowledge on this subject has been acquired only since Reverdin's discovery of "skin-grafting."

The tissues, as is well known, may survive systemic death for a short time. Portions of almost all tissues may be removed from one part or animal and successfully transplanted to another part or animal, if the conditions are suitable. These are:—Transference of the portion of tissue with sufficient gentleness and quickness to ensure that it is alive when transferred: close contact with the raw surface prepared for it: maintenance of its temperature: and the avoidance of all irritation, especially septic. The piece of tissue will, under these circumstances, become united by first intention to its bed, and will be nourished by lymph transuding from this surface until vessels shoot across into it. Naturally, those tissues which are least highly organised and which require the least nutriment bear transplantation best.

Epithelium is the tissue which better than any other bears transplanting. Use is made of this in the operation of grafting, in which small bits of *the superficial part* of the *rete* are placed upon a healthily granulating surface. At first, nourished by the exudation, these fragments grow, adhere, and form centres whence epithelium spreads over the surface. The cells of the root-sheath of plucked-out hairs answer the purpose well. Granulation-tissue may be skinned over in this way; but unless scar-contraction accompanies the skinning over, the cicatrix is liable to break down.

A piece of *skin* an inch square, freed from all fat, may be transplanted, and thus *ectropion* and similar deformities may be remedied.

Similarly, a bit of *mucous membrane,* usually obtained from a rabbit's conjunctiva, is transplanted in cases of *entropion.*

Cartilage and *periosteum,* especially when young, bear transplantation well (see also pp. 122 and 125). So also do bits of *bone.* Macewen, of Glasgow, built up part of an ulna with bits removed from deformed tibiæ, and introduced the practice of replacing chips of the bone removed in the opening made by a trephine.

Pieces of *muscle* have been successfully transplanted, and part of the sciatic *nerve* of a bird has been substituted for a corresponding piece

excised from another bird: the transplantation of nerve has been successful in man, so far as the mere healing-in of a portion of rabbit's nerve placed between the ends of a divided median, but time had not been allowed for restoration of function when the notice was published.

CHAPTER XI.

TUMOURS.

The first notion which the name "tumour" conveys is that of swelling; but swelling may result from very different pathological processes, while the term "tumour" has a much narrower connotation. It is impossible to give an accurate definition of its meaning because its real nature is not understood. It is generally described as a formation of new tissue which is abnormal to the part; which disturbs its form, and differs from it more or less markedly in gross and in minute structure; which performs no physiological function; which tends to continuous growth, and is more or less independent of the general nutrition of the body; and which has not arisen from the causes, or in the course, of inflammation.

That tumours are formations of new tissue necessitates the rejection of all swellings due solely to retention of secretions (retention-cysts), or to extravasation of blood (hæmatomata). True hypertrophies must be rejected because—though they involve an increase in size—the shape, structure, and function are preserved. Finally, all inflammatory swellings, tumour-like products of infective inflammations such as, gummata, tubercles, farcy-buds, and condylomata, and all localised œdemas and effusions—such as hydrocele—must be eliminated.

The definition of a tumour as an *atypical new-formation* would separate the class from retention and extravasation-cysts, and from true hypertrophies; but many an inflammatory new-formation, such as callus or a condyloma, is atypical enough both in form and structure. Moreover, there is a whole group of tumours (sarcomata) which it is impossible to distinguish anatomically from the results of inflammation. It is therefore necessary to include in a definition of tumours something which shall draw the line between them and inflammatory products; such a distinction may be found in their causes, modes of origin, and

progress. We may say, then, that *a tumour is an atypical new-formation, not the result of an inflammation.* False hypertrophies, especially such as affect limited areas (*e.g.*, accumulation of fat on the buttocks of Hottentots), are closely allied to simple tumours, and specially difficult to separate from them.

DEVELOPMENT.—The nutrition of tumours is not regulated like that of normal tissues. When the body gets thin, and the *subcutaneous fat* disappears, a *fatty tumour* wastes but little or not at all; and malignant growths often grow luxuriantly while their victims are rapidly emaciating. With this fact it may be noted that tumours have no nerves, though the relation of nerves to nutrition is as yet little understood.

A tumour consists of cells, formed by multiplication of pre-existing cells, and here, as elsewhere in Nature, the characters of the parent are handed down to the offspring. In other words, a tumour and the cells from which it springs always belong histologically to the same class of tissues (see p. 12).

In development and structure, the tumours resemble the normal tissues—every pathological growth has its physiological prototype. The resemblance, however, is by no means complete, for, as indicated in the definition, they are always more or less **atypical** in their structure. As a rule, the difference between the normal and abnormal tissue is such that with the naked eye one can tell roughly where the one begins and the other ends.

The histological processes which give rise to the formation of a tumour are doubtful in the extreme. It is uncertain whether a tumour grows from a portion of the mature tissues or from a kind of "resting spore" of embryonic tissue as suggested by Cohnheim (p. 125). Evidence of the multiplication of normal tissue-elements round about a growing tumour is often obtainable, but it is very difficult to tell what becomes of them, and Ziegler was inclined to think that most disappeared. A cancer-embolus in a gland almost certainly grows without any additions from the surrounding cells, and there does not seem to be any *a priori* reason why a fibroma or a sarcoma should receive any either.

The elements from which tumours most frequently originate are those belonging to the **common connective-tissue**, and to the blood-vessels and lymphatic system with which it is so intimately associated. By common connective-tissue is meant that tissue which in all parts surrounds the blood-vessels, and is so universally distributed throughout

the entire organism. This must be carefully distinguished from the special varieties of connective-tissue—tendon, cartilage, bone, &c. In this common connective-tissue we distinguish two kinds of cells—the stable or connective-tissue corpuscles, and the mobile or "wander-cells." Both are in intimate relation with the endothelium of the lymphatics, which commence as spaces distributed throughout the tissue. Further, the endothelium of both lymphatics and blood-vessels closely resembles in its physiological functions the fixed cells of the connective-tissue.

Connective-tissue is said to give rise to tumours by multiplication of its cells, the part played by the two kinds being doubtful. Embryonic tissue consists of small round cells with no limiting membrane and a large nucleus, lying in a scanty, semi-fluid, and faintly granular intercellular material. This tissue is often called "indifferent," as it is impossible to determine in this early stage of the growth what it will ultimately become—whether a fibroma, a sarcoma, or an enchondroma, &c.

This "indifferent" tissue now develops into that of the permanent growth, much in the same way as the immature connective-tissue of the embryo develops into various connective-tissue substances—mucous tissue, fibrous tissue, cartilage, or bone. The embryonic tissue may undergo no higher development, the cells remaining round or oval, and the ground-substance homogeneous; or the *nuclei* of several cells may multiply without any corresponding division of the cells themselves, thus forming giant-cells; or most of the cells may lengthen out into spindles, and perhaps here and there fibrillation, with disappearance of some cells, may occur. We thus get the round, oval, myeloid, or spindle-celled sarcoma; also the fibro-sarcoma. General fibrillation with disappearance of most of the *cells*, and mucous degeneration, chondrification or ossification of the *stroma* may occur, thus forming fibroma, myxoma, chondroma, or osteoma; or fat may form in the cells—lipoma. A combination of two or more kinds of structure may be met with in the same tumour—as a combination of sarcoma and lipoma, of enchondroma and myxoma, and so on. We are quite ignorant of the causes, apart from heredity, which determine the ultimate character of the tissue.

Next to connective-tissue, **epithelium**—surface and glandular—is the tissue from which tumours most frequently originate; and as from connective-tissue are produced growths of the connective-tissue type, so growths originating from the epithelia preserve the epithelial type. *A priori*, it would be entirely contrary to evolution for them to

do otherwise; and the great majority of observers state, as the result of their investigations, that epithelium never arises but from epithelium. It is, nevertheless, believed by some that an epithelial cell may by mere contact so influence a connective-tissue cell that it becomes epithelial, or *vice versâ*. This influence of one cell upon another is called "spermatic" (Creighton). The point has been carefully investigated by Ziegler with a negative result.

From the remaining tissues, **muscle** and **nerve**, the development of tumours is comparatively rare; and from the highest adult nerve-tissue it is doubtful if tumours ever arise.

According to the similarity or difference which subsists between the new growth and the tissue from which it grows, tumours are divisible into two classes—**homologous** and **heterologous**. When the tumour resembles in its structure and development the tissue from which it *originates*, it is said to be homologous; when it differs from it, the tumour is said to be heterologous. A cartilaginous tumour, for example, growing from cartilage, is homologous, but growing from any other tissue, as from the parotid gland, it is heterologous. This distinction is probably artificial—not real. If it be correct that tissue-types "breed true," the only even apparent heterology, which we know to occur, is the development of the different connective-tissues from the same embryonic tissue. In the example given, cartilage does not arise from the essential epithelial cells of the parotid, but from the supporting connective-tissue, or from an aberrant bit of cartilage from the rudiment of the jaw. Heterology, however, is not limited to the production of a tissue which is dissimilar from that from which it originates; a tumour is also said to be heterologous (or **heterotopic**) when it differs from the tissue in which it is *situated*, and this may occur without its being the direct product of the latter. It is heterology in this sense that is so characteristic of malignant growths. Cancers, for example, become heterologous owing to the growth and extension of the epithelium beyond its normal limits (see "Epithelioma"); and the same form of heterology obtains in the case of all growths originating from elements which have migrated or been carried from their original habitat, and have developed into a tissue differing from that in which they are found.

RELATION OF THE TUMOUR TO THE SURROUNDING TISSUES.—The relation of the tumour to the surrounding structures varies. In one case the tumour is *circumscribed*,

merely displacing the surrounding parts, and stretching and irritating their connective-tissue; so that this comes to form a fibrous capsule around the tumour, by which it is completely isolated. The lipomata, fibromata, and enchondromata, are usually thus encapsuled. In other cases the growth *invades* the adjacent structures. There is then no line of demarcation between the tumour and the surrounding parts; and although to the naked eye there may seem to be one, the microscope will show that the apparently healthy tissues are infiltrated with a small round-celled growth (Fig. 44), into which the specific tumour-cells are advancing. The former is probably the result of tissue-irritation set up by the latter.

RETROGRESSIVE CHANGES.—A tumour very rarely disappears, and it thus differs from an inflammatory growth—*e.g.*, a

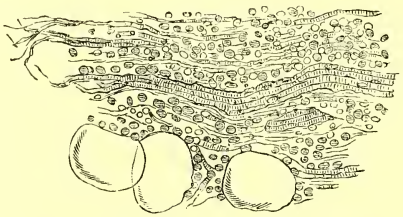


FIG. 44.—*Scirrhus of the Mamma.*—Spreading margin: small-celled infiltration of the muscular fibres and adipose tissue in the neighbourhood of the gland. × 200.

gumma. It may either remain stationary, or grow—slowly or rapidly. Sooner or later it usually becomes the seat of retrogressive changes. The time at which these commence varies. As a rule, the permanence and durability of a tumour bear an inverse relation to the rapidity of its growth and to the inferiority of its organisation. The more rapid the growth and the more lowly organised the tissue formed, the less its durability and the sooner do retrogressive changes occur. The carcinomata and sarcomata develop rapidly, and degenerate quickly. They consist for the most part of cells; their elements are unstable and soon perish. Osseous tumours, on the other hand, develop more slowly, and are but little liable to retrogressive metamorphosis. They consist of a more highly organised tissue, and have much greater stability.

The retrogressive changes are similar to those met with in the

normal tissues. Deficient supply of blood is followed by *fatty degeneration* and its various terminations—softening and caseation. *Pigmentary, calcareous, colloid,* and *mucoid degeneration* may also occur. Tumours may become the seats also of *inflammation, ulceration, necrosis,* and *hæmorrhage.*

CLINICAL COURSE.—Tumours are divided clinically into two great groups, the **simple** and **malignant**. A **simple tumour** is one which, as a rule, grows slowly and steadily, or, having attained a certain size, remains stationary. It consists of tissue approximating closely in structure to some normal adult tissue, and is generally surrounded by a distinct capsule out of which it can be completely shelled—for there is no infiltration of surrounding parts. After such removal it does not recur locally, and secondary growths in glands or more distant parts do not result from it. Its interference with health is only mechanical, unless some accident—as inflammation—occur in it. Tumours of the fully developed connective-tissue type generally pursue this course, and may grow to a huge size.

A **malignant growth**, on the other hand, generally grows rapidly and tends to enlarge continuously. It consists of tissue which is markedly "atypical"; and is, as a rule, surrounded by no capsule, but progressively infiltrates the surrounding tissues. After apparently complete removal it recurs locally, and, whether removed or not, tends to give rise to secondary growths in the nearest lymphatic glands, or in distant parts, or in both. Though the patient is often in excellent health when the tumour first appears, he sooner or later wastes, loses strength rapidly, and becomes very anæmic—*cachexia* is produced. This is due to many causes—*e.g.*, to removal from normal tissues of nutriment required for the active growth of the tumour-cells; perhaps to the metabolism of the latter, pouring abnormal excreta into the blood; to pain and anxiety; often to profuse discharge and septic absorption consequent upon ulceration; and occasionally to actual interference with the ingestion and absorption of food. The more rapidly and the more completely a tumour produces these results, the greater is its malignancy. Even growths of the same class vary much in these respects, and different classes vary still more. Though in a high degree characteristic of cancers, the purely clinical term "*malignant*" must be distinguished from the pathological term "*cancerous,*" which implies a specific structure in the growth to which it refers. Sarcomata are often quite as malignant as cancers.

RECURRENCE AND GENERALISATION.—A tumour may recur *locally* after removal; and either after or before removal, growths similar to the primary tumour may form in the nearest *lymphatic glands,* or in more *distant tissues or organs.* In the highest degrees of malignancy, all these occur. Each must be considered separately.

Reproduction of the Tumour in Adjacent Structures.—This recurrence *in loco* after removal is usually the earliest, and the least important evidence of malignancy. It is due to some of the tumour-cells having been left behind, and is, therefore, much more likely to occur in those growths which infiltrate the surrounding tissues, and *really* extend beyond their *apparent* limits, than in those which are encapsuled. The cells left behind continue to grow and recurrence occurs. Cells may be carried to some little distance from the primary growth by lymph- or blood-currents, and, on becoming impacted, form the nucleus of secondary nodules which may spring up around the original tumour. In some tumours local recurrence occurs many times and often kills the patient without any infection of glands or distant tissues.

Reproduction of the Tumour in the nearest Lymphatic Glands.—This is owing to the entry into, and transmission by, the lymph-stream of cells from the malignant growth, which become arrested in the nearest lymphatic glands, and there develop into secondary tumours. These are in all cases of the same nature as the primary tumour. When the lymphatic glands have themselves developed into secondary growths, they in their turn constitute new centres of infection, and may thus infect the more distant glands or the immediately adjacent tissues. When the lymph-sinuses of a gland are so blocked by new growth that lymph cannot pass, a regurgitant flow is the natural result, and the lymph, bearing tumour-cells, has to pass through abnormal vessels and glands. In this way we can account for infection, say, of the abdominal glands by a tumour of the lung, and for the numerous nodules in the skin which sometimes occur widely all round an atrophied scirrhus of the mamma. A distant lymphatic gland may be infected by embolism of its artery. The tendency of malignant growths to become reproduced in the lymphatic glands varies very much. It is very marked in the carcinomata; while in the sarcomata it is comparatively slight. The reasons for these differences will be seen in subsequent chapters.

Reproduction of the Tumour in Distant Tissues.—This is usually the final stage in the history of malignant growths, and is known

as their "generalisation." The reproduction of the malignant growth in distant tissues is, in the great majority of cases, owing to the entry of some of its elements into the blood-stream. The secondary tumours are therefore the result of embolism of tumour-cells; and the points at which the cell-masses may be arrested are stated in the chapter on Embolism. As in the lymphatic glands, they are in all cases of the same nature as the primary one, although they may be larger and are often softer, more vascular, and more active in growth. They may themselves become secondary centres of infection, and in the same way cause tertiary growths in parts beyond.

Although the general dissemination of a malignant growth is thus in most cases due to the transmission of its elements by the blood-stream, this is not the only way in which it may be brought about. Exceptional cases have been described in which the elements of a tumour have been distributed and have caused secondary growths in other ways, as by passing down the trachea, between the layers of the peritoneum, or from the kidneys down the ureters to the bladder.

Lastly, it must be borne in mind that growths may be secondary to each other only *in time;* that is, they may be entirely independent of each other, originating from different primary foci.

We have spoken of generalisation and lymphatic infection as being due to the transference of tumour-cells from the primary growth. That the primary growth *is* the real source of the secondary growth is shown by their similarity in structure, by their time-relationship, by their demonstrable connection by means of blood or lymph channels, and by the fact that the secondary growths often occur in tissues in which primary tumours of the structure in question never occur. Some authorities think that it is the juice, and not the cells of the primary tumour which is conveyed to the future site of the secondary nodules. But against this view may be urged: the localised action; the distribution of secondary growths in the next capillary area, and the possibility of explaining exceptions to this rule; the occasional discovery of tumour-cells in the blood, most often impacted in the vessels as emboli; the frequent existence of tumours growing into veins and lymphatics, so that cells may easily be swept off by, or migrate into, the stream; and lastly the fact that secondary growths have never been found in cartilage or cornea which are both permeable to fluids.

Two views are held concerning the way in which migrated cells produce secondary growths.

1. It is said that the cells impacted at a certain spot so influence the vessel-wall and surrounding tissues that their cells multiply and produce a structure like that of the infecting particle. The objection has already been stated to this theory of "spermatic influence," which would require us to believe that liver-cells, for example, may by their multiplication produce not only epithelial cells like those of scirrhus or epithelioma, but even connective-tissue cells of all kinds.

2. The cells of the secondary nodule are believed to be the products of the multiplication of the cells of the tumour-embolus. The question thus arises—Can a bit of tumour thus cut off from its base grow? Artificial embolism has been produced with pieces of fresh periosteum, with the result that they grew, and produced first cartilage and then bone; but after the fifth week all trace of them had disappeared. In effect, they went through the same course as do pieces of normal tissue, or of tumour, which are placed in the subcutaneous tissue. We see, therefore, that they can grow; but something in the healthy tissues prevents their attaining any size. On the other hand, a piece of bone or other tissue placed where similar tissue usually exists, does not thus disappear, as transplantation operations show.

THE CAUSES OF MALIGNANCY.—Why do some tumours invade adjacent tissues and distant organs, whilst others do not, even though the latter grow as rapidly as the former? Hitherto difference in structure has been held to explain the matter. The more purely cellular the tumour, the more numerous its blood-vessels, and the less developed their coats, the more rapid is its spread, and the earlier and more certain is its generalisation.

But occasionally we find that a tumour which has run a simple course, and which does not recur after removal, has a structure necessitating its being placed among the sarcomata. Epulides, central sarcomata of bones, and some sarcomata of the ovaries and fasciæ may grow to a large size without invading other tissues or generalising. On the other hand, examples of the generalisation of many simple tumours have been frequently recorded—*e.g.*, chondromata, myxolipomata, and even fibromata; also adenomata of the ovary and thyroid. It is true that connective-tissue growths do generally contain a preponderance of round cells before they generalise; but in some cases the structure of the secondary growths is that of the primary, and is such as is usually seen in specimens which show no malignancy.

Cohnheim thought, therefore, that the essential factor in "malignancy" was not a certain structure on the part of the tumour; but rather some change in the surrounding tissues which rendered them unable to resist invasion. For, from the way in which physiological tissues lie side by side, never invading each other's precincts, though one or both may be growing actively, it is evident that each tissue possesses a power which opposes infiltration by any other tissue; this power Cohnheim called "**physiological resistance**." Its existence is further shown by the results following the artificial production of embolism with pieces of periosteum (p. 122): these results prove that bits of tissue transplanted into the tissues of a normal animal, may become vascularised and grow; but also that they will shortly after disappear—the healthy tissues seeming to regain the upper hand. To permit the infiltration of one tissue by the elements of another, the physiological resistance of the former must be reduced. This may be effected by (1) **Injury**, and therefore in *inflammation;* as in chronic inflammation of epithelium-covered membranes (lupus, chronic glossitis, cirrhosis of liver, interstitial pneumonia, &c.), where masses of epithelium are found in the infiltrated connective-tissue. (2) **Age**: connective tissues grow most vigorously in early life, and sarcomata, which are of the connective-tissue type, are commonest during this period. But the preponderating activity of one form of tissue at one special time is best illustrated by Thiersch, who showed that after mid-life connective tissues atrophy from diminished vital activity; diminished physiological resistance probably accompanies this, and thus the more active surface-epithelium is enabled to invade the sub-lying cutis. This he regarded as essential to the growth of an epithelioma. It is certain that normally epithelial tissues grow most actively in later life, and that the least specialised forms show the tendency last, a fact which may explain why cancer of some organs occurs at an earlier age than that of other organs.* (3) **Heredity**: hereditary weakness on the part of the tissue surrounding a "tumour-germ" must be assumed in young people in whom neither injury nor age can be regarded as a cause of diminished physiological resistance. But even if the power of a tumour to infiltrate is dependent on the presence of this diminished physiological resistance in the adjacent tissues, the structure of the growth probably has also a marked influence upon its malignancy. Tumours which have great power of growth, whose cells are held loosely together, perhaps actually lying

* Woodhead, Morton Lecture, *Brit. Med. Journ.*, vol. i. 1892.

in lymph-spaces, and which possess numerous and thin-walled blood-vessels, must generalise more readily, when this is possible, than tumours in which the opposite conditions obtain.

ÆTIOLOGY.—Little is really known on this point. We have to account for the presence, in the affected tissue, of cells which have capabilities of growth greater than those possessed by the normal cells of the tissue. Increased *food-supply* will of course be required, but this is of secondary importance; so also are the surrounding physical conditions, which may be favourable or unfavourable.

At first, all tumours appear to be local, and **local causes** have consequently been sought. A causal relation seems in some cases to exist between **injury or irritation** and the formation of a tumour. But we know that the effects of these influences on normal tissues are inflammation and hyperplasia, and that they produce these effects even in those who are the subjects of tumours. Further, no history of injury can be obtained in fifteen per cent. of the cases; and the injuries followed by tumours must constitute a very small proportion of the total number of injuries. Still, it is probable that injury, by producing hyperæmia and inflammation, may bring extra food to cells ready to grow, and may diminish the physiological resistance of the tissues round them. Irritation certainly does seem to have a powerful effect in the production of certain epitheliomata: of these rodent ulcers and epitheliomata occurring in old scars or in the scrotum of sweeps are good examples. For the vast majority of cases no local cause can be found.

The cachexia produced by malignant growths, together with their very frequent recurrence, their multiplicity, and their hereditariness—all pointing, it was said, to a deep affection of the whole organism—gave rise to the belief that malignant growths were of **constitutional** origin. This is a bad term, for it may mean "*general*," and refer to the constitution of the whole organism; or it may refer to the constitution of certain cells, and have a *local* significance. We shall therefore use the word *general*. Now, we have already explained that cachexia, local recurrence, and multiplicity may be the results of the growth of a tumour, which was produced by multiplication of a few abnormal cells—*i.e.*, that they may be due to a *local* abnormality. There is therefore no need on these grounds to consider that the physiological processes of all the cells of the organism are abnormal and tend to produce cancer; or that removal of the primary growth

would be useless, because continuance of the general abnormality would reproduce the disease elsewhere. Nor does heredity lead to this conclusion, for the whole of normal development is nothing but the transmission of local peculiarities; and moreover heredity is at least as marked in multiple simple growths—fibromata, warts, lipomata, osteomata—as it is in cancers. It is probable that *all* tumours are at first *local*, and that certain of them become malignant, as above explained; also that any inherited peculiarity, which results in abnormal growth at a certain time, affects only a few cells, or it may be many foci of cells in one tissue, and not the organism at large. It is obvious, however, that neither the constitutional nor the local view makes any pretence at explaining how the abnormal ability to grow is acquired by the cells that give origin to the tumour. Cohnheim advanced a hypothesis, which, if true, would offer a partial solution of the difficulty.

Theory of Embryonic Remains.—On thinking over the hypertrophies, the excessive formations (supernumerary digits and more marked examples of "monster by excess"), the teratomata and other congenital tumours, all of which are admitted to be due to an embryonic cause, many of which are hereditary, and some of which do not appear until years after birth, it occurred to Cohnheim that all tumours might be due to developmental faults. He suggested that more cells than are needed for a part are produced; and that the surplus remain in an embryonic state either in one spot or scattered over a whole tissue. The causes of this error, and the reason why the cells do not develop like their *confrères* and simply enlarge the part, are unknown. We know little of such collections of "resting" embryonic cells, perhaps because of their small size and resemblance to leucocytes. Small nævoid spots may enlarge greatly after birth; congenital moles which have the structure of alveolar sarcomata, may later on become malignant, and islets of cartilage from which tumours may start have been shown by Virchow to occur in the shafts of long bones. Perhaps all these may be regarded as embryonic remains.

Assuming that such embryonic foci may remain among adult tissues, Cohnheim found that his view accorded with observed facts. There would be no difficulty about the reversion of adult cells to the embryonic type; the cells in question would start with their full developmental force. The reasons for believing in the undeveloped nature of the rudiment are—(1) that power of growth is at its greatest in the cells of the embryo, as is shown by the fact that embryonic cartilage, transplanted to the anterior chamber of the eye, grows into a

regular chondroma, whilst adult cartilage is absorbed; (2) that many tumours are obviously distinct from the part in which they lie—*e.g.*, adenoma of the mamma is encapsuled, and its ducts do not open into those of the normal gland; and (3) that tumours are not subject to that regulating mechanism which renders the metabolism of each tissue subservient to the good of the tissues generally.

Moreover, many tumours occur at points where the developmental processes are complicated, and where, therefore, errors are most likely to occur. This is shown by the frequency with which carcinoma affects (1) the openings on the surface of the body; (2) the œsophagus, where it is crossed by the left bronchus (the food and air-passage were originally one here); (3) the cardia, pylorus, and commencement of the pyloric portion of the stomach, where the change of epithelium occurs; (4) the rectum, at the line of union between the invaginated epiblast and the hind-gut; and (5) the external os uteri, where Müller's ducts opened into the uro-genital sinus. Adeno-myomata of the prostate occur at the same spot in the male. Smooth myomata occur almost exclusively in the uterus. The whole uterus is made up of foci of cells awaiting the stimulus of impregnation to great development. Atypical development of one focus may occur without the usual stimulus, and perhaps we should rather expect this when pregnancy has been absent or infrequent; so we find that myomata are commonest in elderly sterile women. Adenomata of the mammæ may be similarly explained.

Heterologous tumours are always so placed that it is possible to see how, by developmental error, some cells which would naturally give rise to the heterologous tissue might have been included in the tumour-germ. Thus, dermoids occur in the neighbourhood of normal invaginations of the epiblast. Muscle may easily get into the Wolffian bodies from neighbouring muscle-plates, and cartilage from the rudiments of vertebræ.

Finally, from so atypical a rudiment, an atypical result might reasonably be expected.

Against Cohnheim's view it may be said that nothing is really known of such embryonic remains; that many of the points of complicated development which he mentions are also points of irritation—*e.g.*, the narrowings of the alimentary canal; and that many tumours of the gullet and rectum, for example, though *near* the points mentioned, are not *at* them. Cohnheim himself was obliged to exclude from this class of tumours such cases as epithelioma of scars, of the scrotum in

sweeps, and of the arm in paraffin-workers, in all of which irritation plays so obvious a part.

The concurrence of **increased blood-supply** is evident in many cases—*e.g.*, enlargement of ovarian dermoids at puberty, of tumours of the breast, ovaries, and uterus in pregnancy. This may cause the multiplication of cells capable of growth, and may explain the apparent causation of tumours by injuries.

Parasitic Theory.—Malignant growths—Carcinoma and Sarcoma—in their obscure origin, their tendency to spread locally, and their dissemination by lymph and blood paths, present so obvious a resemblance to certain infective diseases, such as tuberculosis, that, the parasitic nature of these infective diseases having been demonstrated, the malignant growths are naturally suspected of having the same ætiology. Some pathologists lean strongly to the view that these growths begin by the inoculation at some spot of some parasite which excites the cells to rapid multiplication, and believe that infection takes place from this focus by the conveyance of the parasite along the lymph and blood paths. In the somewhat unusual cases of a general outbreak of malignant growths, it is assumed that the primary focus, in which the poison was received and multiplied, was not recognised; a parallel can be established between them and cases of general tuberculosis in which no primary focus is found.

The "constitutional theory" is also resuscitated, but it is now made to correspond to the "tubercular diathesis," or predisposition of certain tissues to permit the growth of the bacillus tuberculosis. It is no longer supposed that all the tissues of a cancerous patient are tending to grow cancerously, or throwing something into the blood which "will out" somewhere, but merely that certain tissues will permit the growth of the hypothetical parasite, should it ever reach them. This "malignant predisposition" may be inherited or acquired; it may be so strong that nothing is required for the production of a malignant growth but the arrival of the germ at a predisposed spot. In other cases the physiological resistance of the tissues may require still further depression by injury or privation before they will permit the multiplication of the germ in their midst: the effect of irritation and injury in cases of tubercular disease following bronchitis or strain of a joint, and those of cancer following irritation by soot, tar, or a blow. Irritation is, upon this view, in the case of cancer, held to depress the vitality of the **epithelium**, and to cause it to admit to its own substance a germ previously resisted; and the frequent origin of cancer of the breast, at

the menopause, when the breast-epithelium is degenerating, is quoted in support of it. The analogy between cancer and tubercle may be traced into even finer details: thus both, when they affect the face (rodent ulcer and lupus), take an unusual course—slow ulceration without any affection of glands or of distant parts and without any accompanying "cachexia."

It is further suggested in favour of the parasite theory, that the absorption of the products of bacterial decomposition would help to explain the cachexia, and might account for the fever which accompanies the growth of some tumours, especially lymphomata; and that both the alleged incompatibility, so to speak, of active tubercular and cancerous disease in the same subject, and the rare disappearance of a malignant growth after a fever, especially erysipelas, may be due to the triumph of one organism over the other in the struggle for existence.

The presence of specific parasites in emboli derived from tumours would, it is said, explain the growth of secondary tumours without the aid of any special diminution of the physiological resistance of the tissues in which the embolus lodges.

Lastly, there is a small number of cases recorded in which cancer of one labium has caused cancer of the opposing surface, and Cripps mentions a case of cancer of the arm resulting from contact with an ulcerating scirrhus: these are regarded as proving inoculability.

This concludes the *a priori* case which has been made out for the parasitic origin of tumours. There is but little positive evidence in its favour. Gussenbauer alleged that he had discovered the cause in certain minute highly refracting particles in and between the cancer-cells. Observers have uniformly failed to find any parasite by means of the *ordinary* staining methods, or by means of cultivations. Shattock and Ballance published the results of cultivations from a large number of tumours—malignant and simple—in which no antiseptic (that might kill any germ) was used: but their cultivations remained sterile. They concluded that if the parasite is a protophyte it must be of a very special kind, and inclined to the view that it is probably a protozoon, which either exercises a "spermatic influence," or lives as a true parasite in the epithelial cell, or, by conjugating with an epithelial cell, confers upon it fresh life and power of multiplication.

During the last few years, many observers have found in the epithelial cells of cancers what they believe to be parasitic protozoa. These

"cancer bodies" will be described and figured in the chapter on carcinoma. Their features have many points in common with the coccidia known to produce marked epithelial proliferation in the rabbit's liver: the absence of spores, however, constitutes a notable difference. Ineffectual efforts have been made to supplement the purely anatomical evidence. The capsule of encysted protozoa is believed to consist of chitin or of cellulose; but careful analysis of cancerous growths fails to establish the presence of either of these. No one has yet succeeded in separating or cultivating these supposed parasites.

Inoculations of cancer-juice upon man and animals fail not only to produce the disease but even any inflammatory reaction; though, on the other hand, it is argued, with fairness, that to produce the disease predisposition may be required.

In spite of the resemblance between the modes of spreading and the consequent morbid anatomy of the malignant growths and tubercle—which really goes for very little—and of the plausible nature of the other arguments adduced in favour of the parasitic origin of malignant growths, the probability seems to us to be as much against as in favour of it, at least as regards the true cancers. In the infective granulomata, bacilli carried by the lymph or blood-stream lodge and excite an inflammation similar to that which they caused at the primary focus: the cells of the granuloma are chiefly leucocytes—not the progeny of cells from the primary focus—and the tendency of the cells of granulomata, even when supplied with blood, is never to multiply indefinitely. It has hitherto been believed that secondary sarcomatous growths were truly the progeny of the primary growth—formed by multiplication of cells carried from the primary focus; and the melanotic nature of the secondary growths in melano-sarcoma has generally been regarded as proof of it, there being no positive evidence of "spermatic influence" (p. 117). But, as sarcoma-tissue is indistinguishable from inflammatory tissue, and as our beliefs as to the origin of sarcoma-cells are based on inferences, and not upon direct observation, it is possible that we are mistaken as to the nature of some morbid sarcoma-like processes, and that we shall find them to be inflammatory and to depend upon an infective cause, like Rhinoscleroma. With regard to the epithelial multiplication which characterises true cancer, however, there can be no such mistake: the immediate cause of cancer must induce this. The question then arises—is it conceivable in the face of the necessarily deleterious action upon their host of all parasites, that this cause can be a parasite?

Reviewing the whole question, it is obvious that we have only more or less probable surmises before us. With regard to *simple tumours,* Cohnheim's theory of "embryonic remains," which brings them into relation with "monsters by excess," seems to be the most likely. As to *true cancers,* the view that the physiological resistance of the connective-tissue is reduced until epithelium, having, perhaps, only its normal tendency to grow, can invade it, appears to accord best with known facts: unusually rapid multiplication of epithelium would then naturally result from increased food-supply. As to the ætiology of the sarcomata, there is even less ground for surmise.

CLASSIFICATION. — Tumours having the most obviously similar structure vary much in their clinical history, whilst others of radically different structure have very similar physical signs and courses. In our present state of ignorance no satisfactory classification of tumours is possible. The one we shall adopt is based upon their histological characters. Tumours arising from *mesoblastic* tissues will be arranged in three groups; the *first,* resembling the most highly differentiated tissues; the *second,* the ordinary connective tissues; and the *third,* the embryonic tissue. In dealing with tumours from *epiblastic* and *hypoblastic* tissues the same order will be followed.

For convenience sake, all cysts will be grouped together and remarks on them made at the end of tumours—though the great majority of cysts are not tumours.

Classification of Tumours.

Mesoblast.

I.—*Type of Higher Tissues.*

Type of muscle	Myoma.
,, nerve	Neuroma (*see* Note on p. 132).
,, blood-vessels	Angioma.
,, lymphatic vessels	Lymphangioma.

II.—*Type of Fully-developed Connective Tissues.*

Type of fibrous tissue	Fibroma.
,, mucous ,,	Myxoma.
,, adipose ,,	Lipoma.
,, cartilage	Chondroma.
,, bone	Osteoma.
,, lymphoid tissue	Lymphoma.

III.—*Type of Embryonic Connective-Tissue.*

The varieties of Sarcoma.

IV.—*Type of Epithelial Tissues.*

Epiblast and Hypoblast.	Papillæ of skin or mucous membrane . . .	Papilloma.
	Glands	Adenoma. Carcinoma.

V.—*Teratomata, or Congenital Mixed Tumours.*

CHAPTER XII.

THE MYOMATA, NEUROMATA, AND ANGIOMATA.

THE MYOMATA.

The **Myomata** are tumours consisting of muscular tissue. There are two varieties—the striated and non-striated.

1. The **Striated Myomata** consist of striated muscle. They are exceedingly rare, only two or three examples having been recorded, and these were congenital. Striated muscle-cells, generally mixed with a few non-striated, occur in the sarcomata of the kidney and testis found in young children. Striated muscle-cells in congenital growths of organs developed from the Wolffian body are probably due to inclusion, in this body, of cells from the adjacent muscle-plates.

2. The **Non-striated Myomata** are most frequent in the uterus; they occur also in the prostate, the œsophagus, the stomach and the intestines. They frequently become pedunculated and form polypi. They are much commoner than the striated growths, and probably always originate from muscle. They may form distinctly circumscribed tumours surrounded by a fibrous capsule, or ill-defined irregular masses in the midst of the muscular tissue in which they grow.

They consist, like the physiological tissue, of elongated spindle-cells, with rod-shaped nuclei, more or less isolated or grouped into fasciculi of various sizes, with a varying quantity of connective-tissue. The muscular elements either present a more or less regular arrangement, or pass in all directions through the tumour. The blood-vessels which usually are not numerous, are distributed in the connective-tissue.

The most frequent **secondary change** which myomata undergo

is **calcification. Hæmorrhage, mucoid softening,** and the formation of cysts, are occasionally met with; also **inflammation,** ulceration and necrosis.

Clinically, the myomata are perfectly innocent.

Myoma of Uterus.—The uterus is by far the most frequent seat of myomata, and here they constitute the so-called "uterine fibroid." In most of these muscular tumours of the uterus there is a large proportion of connective-tissue—hence the terms "fibroid" and "fibro-myoma." This is the case especially in older growths. Those newly developed, however, consist almost entirely of true muscular tissue. They either form firm hard masses, embedded in the uterine walls, or project into the uterine or abdominal cavities. When projecting into the uterus they constitute a common form of uterine polypus. They do not form till after puberty, and are commonest in elderly sterile females. Their growth is usually slow. Pregnancy causes them to enlarge rapidly, and they undergo some involution after delivery. They generally atrophy at the menopause. These tumours are often multiple. The older ones are liable to become calcified. They also sometimes undergo mucoid softening, which gives rise to the formation of cysts in their interior.

THE NEUROMATA.*

The **Neuromata** are tumours consisting almost entirely of nerve-tissue, and are among the rarest of new growths.

The term **"false neuroma"** has been applied to many growths found in connection with nerves. Fibrous, myxomatous, and gummy tumours growing within the nerve-sheath have been included under this head. Small multiple fibromata of superficial nerves are sometimes hereditary. The bulbous ends of nerves in stumps are by some called **amputation-neuromata.** They often consist only of fibrous tissue, but may contain rolled-up nerve-fibres—attempts at regeneration rather than a tumour. They are usually intimately connected with the cicatricial tissue of the stump.

The structure of true neuromata is most commonly that of a mass of ordinary medullated nerve-fibres; they therefore resemble in structure the cerebro-spinal nerves, from which they most frequently grow.

* If, as seems probable, nerves are outgrowths from the cerebro-spinal centre, true neuromata should be classed as epiblastic growths.

The nerve-fibres are associated with more or less connective-tissue. Virchow has also described as exceedingly rare formations tumours composed of non-medullated fibres and of ganglionic nerve-tissue.

Neuromata rarely attain a large size, but usually exist as small, hard, single nodules.

True neuromata always originate from pre-existing nerve-tissue—either from the cranial or from the spinal nerves. This fact determines their site.

Clinically, the neuromata are perfectly innocent tumours. They often cause considerable pain. Their growth is slow.

THE ANGIOMATA.

The **Angiomata**, or vascular tumours, consist of blood-vessels held together by a small amount of connective-tissue.

This group includes the various forms of nævi, and aneurysm by anastomosis. They may be divided into two *varieties*—the **simple** or

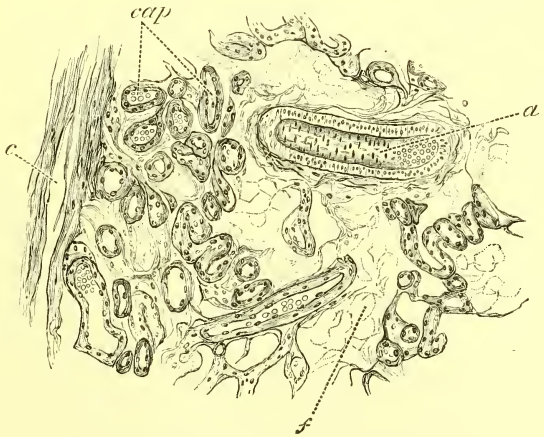


FIG. 45. — *Capillary Nævus from Subcutaneous Tissue of a Child.* *cap.* vessels of new growth; *a.* normal artery; *f.* fat-cells; *c.* capsule. × 200. Reduced ½. (Boyd.)

capillary angiomata, in which the new vessels resemble chiefly normal capillaries; and the **cavernous** or **venous** angiomata, in which the blood circulates in a cavernous structure similar to that of the corpus cavernosum of the penis. The characters of both are well shown in the accompanying Figs. 45 and 46.

1. **Simple Angiomata.**—These consist of tortuous and dilated capillary vessels, held together by a small quantity of connective- and adipose-tissue (Fig. 45). It is doubtful what proportion of the vessels is due to dilatation of the original capillaries: Ziegler thinks that many are formed this way. Some are of new formation. Very irregular dilatations are common. The capillary walls may be thin or thick, consisting of a double tier of cells. One or two supplying arteries can be seen in most sections. These growths generally occupy

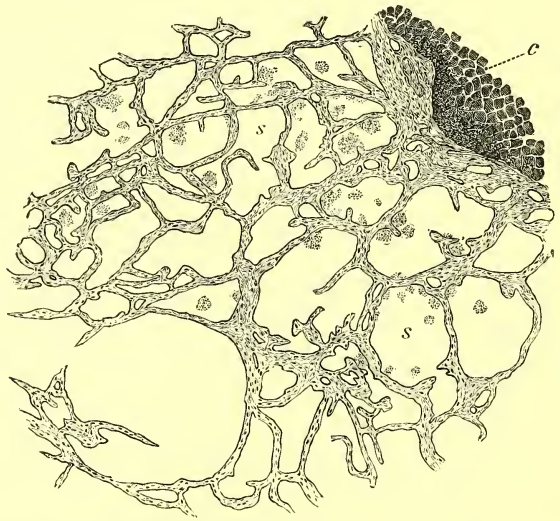


FIG. 46.—*Cavernous Nævus of Liver.* From a woman aged 39. *ss.* Large spaces bounded by fibrous walls, some containing blood débris; *c.* liver-cells (too large) toward which the growth is bounded by thick fibrous walls. × 40. Reduced $\frac{1}{3}$. (Boyd.

the superficial layers of the cutis, and form the port-wine stains and mother's marks; they are slightly or not at all elevated. Others lie in the subcutaneous or submucous tissue, and may form large tumours. Their colour is red, violet, or purple, according to the depth of the vessels from the surface and the rate of flow through them; the most frequent colour is red when superficial, bluish when subcutaneous. They are probably always congenital, though they may not be noticed for a few weeks after birth.

Simple angioma is often combined with lipoma, glioma, or sarcoma. Sometimes cysts, containing dark fluid, form in them.

2. **Cavernous Angiomata.** — These are the venous tumours. The growth is made up of irregular fibrous alveoli, which communicate freely with one another, and are lined with an endothelium similar to that of the veins (Fig. 46). These spaces are distended with blood, which is supplied to them by numerous tortuous vessels and circulates with varying degrees of rapidity. The arteries open directly into the spaces. These growths are commonly of a bluish colour. They may be diffuse, or form distinctly circumscribed tumours. They sometimes exhibit distinct pulsation. Their favourite seat is the skin and subcutaneous tissue. They may occur also in the orbit, muscle, liver, spleen, and kidneys. They may develop by dilatation of the vessels of a simple angioma. They may be congenital; but in the liver Ziegler thinks they develop after middle age, when the cells begin to atrophy.

Aneurysm by Anastomosis.—The arteries of an area, especially on the head, become dilated, greatly elongated, and tortuous; perhaps new vessels form. Some are congenital, others follow injuries.

Lymphangiomata.—See p. 150.

CHAPTER XIII.

CONNECTIVE-TISSUE TUMOURS.

THE FIBROMATA.

The **Fibromata** consist of some form of fibrous tissue.

The **fibres**, which constitute the chief part of the growth, are either loosely or densely packed according to the variety, and are arranged either without definite plan, or in intercrossing bundles of various sizes, or in whorls around the blood-vessels (Fig. 47). Yellow elastic fibres are very rarely met with. The **cells**, like those of normal fibrous tissue, are generally few in number, and are usually most abundant around the vessels. They are minute, spindle-shaped, fusiform, or stellate bodies, the latter having processes of varying length, which communicate with similar processes from neighbouring cells. In the fresh specimen the cells are often so small and indistinct as to become visible only after the addition of dilute acetic acid. These cells vary in size and number with the rapidity and age of growth—the slower and older the growth, the denser the tissue, and the flatter and less numerous the cells.

The fibromata usually contain but few blood-vessels. In the softer growths, however, these are often more numerous. Dilated veins sometimes form a cavernous network, the walls of which are firmly united to the tissue of the tumour, so that if divided or ruptured they are unable to retract or collapse, and profuse hæmorrhage may thus ensue.

Partial **mucoid softening** and **calcification** are the most common **secondary changes**; ossification occurs in fibromata springing from bone. **Ulceration** also sometimes occurs in those growths which are situated in the skin and submucous tissues.

Fibrous tumours present **two varieties**, the **soft** and **hard**, corresponding to, and usually originating from, the loose and dense varieties of ordinary connective-tissue respectively.

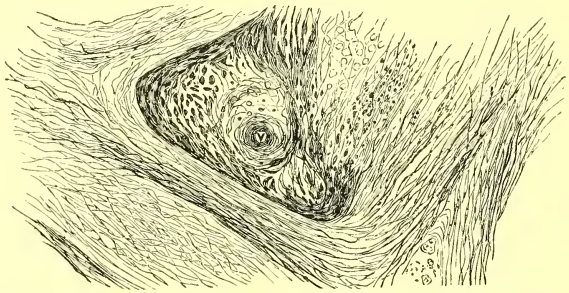


FIG. 47.—*Fibrous Tumour from the Skin.* Near the cut blood-vessel, V, are seen some cells; also fibres cut transversely. × 200 and reduced ½.

1. **Soft Fibromata.**—These consist of the looser and less dense form of fibrous tissue. They are met with as diffused growths in the subcutaneous and submucous tissues. In the former situation they often form large pedunculated and non-encapsuled tumours, which are commonly known as **wens**. These are sometimes multiple. A similar growth of subcutaneous tissue is met with in **molluscum fibrosum**. In this disease the large masses which hang down from the thighs, buttocks, and other situations consist entirely of loose fibrous tissue. They often contain many large blood-vessels, so that their removal may lead to severe hæmorrhage.

In addition to these diffused growths, more circumscribed and **encapsuled** fibrous tumours of the soft variety are occasionally met with growing from the scalp, scrotum, labium, intermuscular septa, or other situations.

2. **Hard Fibromata.**—These are composed of dense fibrous tissue, like that in tendons. They are firm, hard, encapsuled tumours, presenting on section a greyish-white, glistening, fibrous appearance. These tumours often occur in connection with bone—especially the upper and lower jaws—originating either in the centre of the bone, or in the periosteum. Growing from the periosteum of the alveolus they constitute simple fibrous **epulis**. They are also met with in the nose, where they form one variety of **nasal polypus**, and in the naso-pharynx, springing from the front of the spine, or from the base of the skull. In these firm fibrous growths the veins may form cavernous spaces.

Another variety of hard fibrous tumour grows in connection with nerves, and is often described as a **neuroma**. True neuromata, however, are, as has been said, among the rarest (p. 132) of new growths. These false neuromata most frequently occur in connection with the superficial nerves. They grow from the neurilemma, and as they increase in size the nerve-fibres become expanded over them. They are very firm rounded tumours, and are frequently multiple and hereditary.

Some old tumours of the uterus are almost or quite pure fibromata; but the so-called uterine "fibroids" are in most cases local overgrowths of the involuntary muscular tissue of the organ (p. 132).

The fibromata **originate from connective-tissue**: from the cutis or subcutaneous tissue, from submucous or subserous tissue, from fascia, from periosteum, from neurilemma, or from the connective-tissue of organs.

Clinically, the fibromata are perfectly innocent: they grow slowly, and do not recur after removal.

Psammoma.

The most characteristic feature of this rare growth is that it consists largely of calcareous particles. These are contained in the concentric bodies already described as the corpora amylacea, where they give rise to the so-called "brain sand"—hence the name of the growth. The calcified corpora amylacea are held together by a varying quantity of loose fibrous, highly cellular, or mucous tissue containing vessels.

Psammomata grow from the pineal gland, the membranes of the brain, or the choroid plexus. In the latter situation a psammoma

often contains numerous cysts. It is of no pathological importance except when of sufficiently large size to produce symptoms from pressure.

THE MYXOMATA.

The **Myxomata** consist of mucous tissue—*i.e.*, a fragile connective-tissue of which the intercellular substance is translucent, homogeneous, and jelly-like, containing much fluid, and yielding mucin. Physiologically, this tissue is met with in the *vitreous body* of the eye, in which the cells are roundish and isolated; and in the *umbilical cord*, in which the cells are fusiform or stellate, and give off fine anastomosing prolongations. All embryonic connective-tissue (p. 65) possesses an intercellular substance containing much mucin, especially that which subsequently becomes adipose. New formations may undergo mucoid degeneration, and thus closely resemble in their physical and chemical characters the myxomata; but a myxoma consists of mucous tissue from the first. The myxomata are thus very closely allied to the sarcomata, and by many are included in the same class of new formations. An œdematous fibroma or lipoma closely resembles a myxoma or myxo-lipoma: Köster believes that they are identical.



FIG. 48.—*Myxoma.*—From the arm: showing the characteristic branched anastomosing cells, a few leucocytes, and one or two spindle-cells. × 200.

Structure.—The majority of the cells are angular and stellate, with long anastomosing prolongations; others are isolated, and fusiform, oval, or spherical in shape (Fig. 48). Their contour is very indistinct, owing to the refracting nature of the intercellular substance. The latter is very abundant, perfectly homogeneous, soft, gelatiniform, viscid, and yields large quantities of mucin; in it are a varying number of amœboid cells. Blood-vessels are not numerous, and are readily visible and easily isolated. A few elastic fibres are sometimes seen between the cells.

Among the **secondary changes** the most common is rupture of the capillaries, **hæmorrhage**, and the formation of **blood-cysts**; this, however, is less frequent than in the sarcomata. The cells them-

selves may undergo **mucoid** or **fatty degeneration**, and thus be destroyed: this is usually accompanied by liquefaction of the intercellular substance. The growth may **inflame**, ulcerate, and necrose.

The **varieties** of myxoma depend principally upon its combination with other growths; a pure myxoma is very unusual. The most common combination is a myxo-lipoma. Combinations with sarcoma, fibroma, chondroma, and adenoma are also met with.

To the **naked eye**, the myxomata are of a peculiar soft gelatiniform consistence, and of a pale greyish or reddish-white colour. Their cut surface yields a tenacious mucilaginous liquid, in which may be seen the cellular elements of the growth. They are usually separated from the surrounding structures by a very thin fibrous capsule. Fine prolongations extend from this into the growth, dividing it into lobules of various sizes. In exceptional cases a myxoma may increase by the continuous invasion of the surrounding tissues.

Myxomata **grow from connective-tissue**, and are most common in subcutaneous and subserous fat, and in submucous and intermuscular tissue. They also grow from the periosteum and medulla of bone, from the connective-tissue of organs (especially the breast), and from the *perineurium* of nerves, forming one variety of "false neuroma." They may grow from the placenta, constituting the so-called "uterine hydatids."

When situate in superficial parts they may become pedunculated: in the submucous tissue of the nose they constitute one form of nasal polypus. In the skin they are often papillary.

Clinically, myxomata occur chiefly after mid-life, and are, for the most part, benign. Their growth is usually slow, but they may attain an enormous size. If completely removed they rarely recur. Sometimes, however, they recur locally after removal, but they probably never reproduce themselves in internal organs. In speaking of their malignancy, their occasional association with sarcoma must be borne in mind.

THE LIPOMATA.

A **Lipoma**, or fatty tumour, is a localised and circumscribed formation of fat.

The lipomata resemble in their **structure** adipose-tissue (Fig. 49). They consist of cells containing fat, and a variable quantity of common connective-tissue. The cells are like those of adipose-tissue, though

usually somewhat larger. The nucleus and protoplasm are so compressed against the cell-wall by the fluid contents, that they are readily visible only when the cell is atrophied and contains less fat (Fig. 5, p. 30). Connective-tissue varies much in amount, unites the cells in masses or lobules which are larger than normal, and forms in most cases around the tumour a thin capsule more firmly adherent to surrounding parts than to the tumour; so the latter, in most cases, "shells out" easily. Blood-vessels are distributed in the fibrous septa. Mucous tissue is often associated with the fatty (myxo-lipoma).

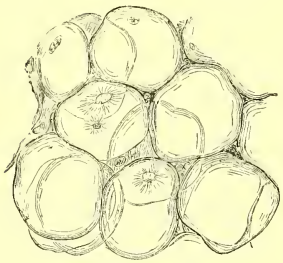


FIG. 49.—*Lipoma.*—Some of the cells contain crystallised fatty acids. × 200.

Secondary changes in the lipomata are not common; their fibrous septa, may, however, become **calcified**, or even **ossified**. Softening may occur also from a **mucoid** change. **Inflammation** is rare; but when large and situated in the subcutaneous tissue the skin over them may become adherent, and ulceration and necrosis of the tumour occur.

The chief **varieties** are the **fibro-lipoma**, in which the fibrous tissue is excessive, and the **myxo-lipoma**, or combination of mucous with fatty tissue. For **lipo-sarcoma**, see p. 153.

To the **naked eye** the lipomata are more or less lobulated, and usually surrounded by a fibrous capsule. When subcutaneous they move freely over the deep fascia; but often the attempt to raise the skin from them causes it to dimple. On section they present the ordinary appearance of adipose-tissue, with more or less dense fibrous septa between the lobules. Their consistence and their adhesion to the capsule vary with the amount of fibrous tissue which they contain. In their growth they occasionally become pedunculated.

Lipomata **grow from connective-tissue**, and their possible distribution is almost co-extensive with that of adipose- and connective-tissue. They occur most frequently in the subcutaneous tissue of the trunk, especially of the back and abdominal wall; sometimes in intermuscular septa, subsynovial and subserous tissues; and occasionally also in the submucous tissue of the stomach and intestines, and even in internal organs where there is normally no fat.

Clinically, the lipomata are quite innocent; they grow slowly, but may attain a huge size; they are usually single, but are not infrequently

multiple and hereditary. Sometimes they change their position considerably, presumably from the influence of gravity.

THE CHONDROMATA.

A **Chondroma** is a tumour composed of cartilage.

In **minute structure** these tumours consist of cells and of an intercellular substance, both of which present all the variations observed in normal cartilage. The **intercellular substance** may be hyaline, fibrous, or mucoid. When fibrous, the fibres may be arranged like those of fibro-cartilage, or more or less concentrically around the cells, as in the reticular cartilages of the ear and larynx (Fig. 50). The fibres may be distinct or hardly perceptible. When hyaline or mucoid, it is sometimes quite soft in consistence. The **cells** may be numerous, or few in proportion to the matrix In the fibrous forms they are often small, and even somewhat spindle-shaped, more resembling those of connective-tissue; in the hyaline forms they are usually large, and either round or oval (Fig. 51); and in the rarer mucoid forms they are more commonly stellate and branched, like the transitional cells at the edge of articular cartilages where the synovial membrane ends. They are either single or arranged in groups, and are usually surrounded by a capsule, as in normal cartilage, although this is often very indistinct. They enclose one or more nuclei and slightly granular contents; sometimes a cell-wall cannot be distinguished.

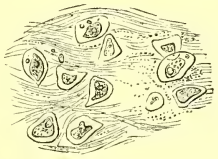


FIG. 50.—*Fibrous Chondroma.* × 200.

Calcification is the most common **secondary change**. It affects with peculiar frequency the largest group of chondromata—those of the metacarpals and phalanges of the hands. It spreads from many centres, commencing in the capsules, and then involving the intercellular substance. **Ossification** is especially frequent in the chondromata which grow near the junctions of the epiphyses and shafts of long bones. These ossify as they grow, and form the pedunculated exostoses. So also does the common sub-ungual exostosis of the great toe, which is generally an ossifying fibroma, chondroma, or fibro-chondroma. **Fatty degeneration** and **mucoid softening** are common changes, and may lead to the formation of large softened masses which present the appearance of cysts. In rare cases the skin covering the tumour ulcerates, and a fungating mass protrudes.

The **varieties** of chondroma depend upon the nature of the intercellular substance, and are therefore **fibrous**, **hyaline**, and **mucoid**; these are often combined in the same tumour. As a rule those originating from the medulla of bone are of the hyaline and mucoid class, whilst those originating from connective-tissue in other situations are more frequently fibrous. The rapidly growing fibrous forms approach very closely to the sarcomata (**chondro-sarcoma**), the mucoid forms to the myxomata (**myxo-chondroma**); and these two kinds of growth are often associated in the same tumour. Chondromata are rarely homologous in the strict sense (p. 117).

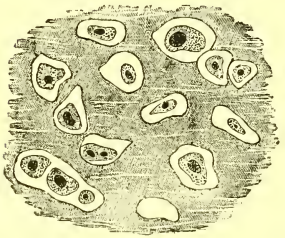


FIG. 51.—*Hyaline Chondroma.* × 200.

A variety of chondroma has been described under the name of **osteo-chondroma**, which in structure more closely resembles bone than cartilage. It consists of a tissue similar to that met with between the periosteum and bone in rickets, which, from its resemblance to osseous, has been called **osteoid** tissue. This only requires calcifying to become true bone. Like bone, it is made up of trabeculæ and medullary spaces; but the trabeculæ, instead of being formed of bone-corpuscles and lamellæ, consist of small angular cells without a capsule, situated in an obscurely fibrillated matrix, which in part is calcified. The medullary spaces contain a fibrous stroma and many blood-vessels. The osteo-chondromata, although consisting mainly of this osteoid tissue, contain also a small proportion of cartilage. They originate beneath the periosteum, their common seat being the ends of the long bones. Their growth is very rapid, and they often attain an enormous size. They are much more freely supplied with blood-vessels than the ordinary chondromata, and hence they are much less frequently the seats of retrogressive changes. They are especially prone to become ossified, and to be thus converted into true bone.

To the **naked eye** the *more slowly growing* chondromata are hard or slightly elastic tumours, smooth or lobulated, and seldom exceeding the size of an orange. They are encapsuled, and consist either of a single tumour or of several smaller masses held together by fibrous tissue in which the few blood-vessels run. On section they present the appearance and consistence of hyaline or fibro-cartilage, frequently modified by one or other of the secondary changes above mentioned. The

appearances may be those of a fibroma, the cartilage cells being unrecognisable without the aid of the microscope.

The *more rapidly growing* forms, such as often start from the pelvic bones or ribs—myxo-chondromata, osteo-chondromata and chondro-sarcomata—are much larger, softer, and more vascular, and never present the appearance of pure cartilage; only a few islets, at most, will be distinct in the soft greyish tissue, which is not separated by any capsule from the adjacent tissues.

Chondromata most frequently **grow from common connective-tissue** and **bone,** *very rarely* from cartilage. About *three-fourths* of them start in connection with bones, growing either *centrally* or *subperiosteally.* Their favourite seats are the bones of the fingers and toes, the lower end of the femur and the upper ends of the humerus and tibia. Much less often, the ribs and the hip-bone are attacked. Virchow has shown that islands of cartilage not uncommonly remain in the shafts of bones; and it is probable that many chondromata spring from such islands (p. 125). The tumours generally begin before the ossification of the epiphyses, whilst the bone is actively growing and vascular.

Most of *the remaining fourth* occur, in combination with other tissues, as "mixed tumours" in the **parotid** and **testicle.** Cohnheim suggests, as the source of cartilage in the parotid, an aberrant bit of the rudiment of the jaw; Virchow, a piece of the pinna. In the testis a portion of the rudiment of a vertebra may have been included. The inter-muscular septa, the subcutaneous tissue of the breast, and the lungs, are occasional seats.

Lastly, cartilaginous growths may originate from **cartilage** itself (**ecchondroses**). These are sometimes seen on the surface of the articular cartilages, in the larynx and trachea, and on the costal and intervertebral cartilages. They are simply local overgrowths of hyaline cartilage.

Clinically, the chondromata are for the most part innocent growths. They are usually single, except when occurring on the fingers and toes, in which situation they are more frequently multiple. The *central* growths of the phalanges and metacarpals occur in children, or before ossification is complete: the graver, *subperiosteal,* forms are commoner later on.

The softer forms, especially those starting from bone and glands, occasionally exhibit more or less malignancy—tending to recur locally and, rarely, to infect the lungs and even other parts.

THE OSTEOMATA.

The **Osteomata** are tumours consisting of bone, either compact or cancellous.

The osteomata are the result of the ossification of *newly formed connective-tissue*, other than of inflammatory origin. They must be clearly distinguished (1) from the simple *ossification of normally existing tissues, e.g.*, costal, laryngeal, or bronchial cartilages, insertions of muscles (rider's bone in adductor longus and the like), and membranes of the brain; and (2) from similar *ossification of inflammatory tissue*—such as nodes or general thickenings of bones, the sharp stalactitic processes which may grow round a carious joint or on the surface of bone, and the smooth round prominences which almost encircle a joint in rheumatoid arthritis. They must be distinguished, also, from *calcareous deposits* in which there is no bone formed (p. 83).

Osteomata are generally divided into two main **varieties**.—1. **Homologous osteomata**, subdivided into **exostoses** and **enostoses**, according as they project from the surface or into the medullary canal of a bone. 2. **Heterologous osteomata**.

1. **Homologous osteomata**: *a.* **Exostoses** are divided, according to the density of the bone of which they consist, into two kinds—(*α*) the *compact, ivory,* or *eburnated;* and (*β*) the *cancellous* or *spongy*.

(*α*) The **ivory exostosis** grows from periosteum. It occurs most frequently on the external and internal surfaces of the skull: the orbit is an especially favourite seat. It is met with also on the scapula, pelvis, and on the upper and lower jaws. In the last-named situation it may grow from the dental periosteum.

Such growths are smooth, low, rounded, wide-based, covered by the periosteum, and continuous with that of the old bone, from which they grow. On section they are throughout of ivory-like density, and they are usually well-defined from the adjacent tissue. Microscopically, the lamellæ are arranged concentrically and are parallel to the surface of the tumour; cancellous tissue is absent, and Haversian canals are few and narrow. Some specimens are less dense, the Haversian canals being as numerous as in ordinary compact bone, but less regularly arranged.

(*β*) The **spongy** or **cauliflower exostosis** is really an ossifying chondroma. It grows from cartilage, usually near the junction of an epiphysis of a long bone with the shaft. It is especially common at the lower end of the femur, and at the upper ends of the tibia and humerus. Its outline is less regular than that of the ivory growths:

but it is prominent, more or less pedunculated, and, so long as it is growing, covered by a cap of cartilage. When this cap ossifies, growth ceases. A section shows that the mass consists of spongy bone, directly continuous with the cancellous tissue of the bone whence it springs, and surrounded by a thin layer of compact bony tissue. The medullary spaces may contain embryonic, fibrous, or fatty tissue.

(*b*) The **enostosis** is a dense bony growth projecting into the medulla, and is very rare.

2. **Heterologous osteomata** are very rare as primary growths. They have been described as occurring in the subcutaneous tissue; but Malherbe has shown reason for believing that such growths are really sebaceous adenomata with ossified stroma (p. 171). Bony tumours have very rarely been found in the brain and cerebellum. Parts of fibromata, lipomata, and chondromata may ossify. The secondary growths of ossifying sarcomata connected with bone often ossify.

The commonest **secondary change** is **inflammation**. Osteomata may also become carious or necrose. The last change is most likely to occur in ivory exostoses, effecting their separation and cure.

Osteomata generally **grow in connection with bone** (homologous), commencing in the periosteum, medulla, or persistent islands of cartilage; but **connective-tissue tumours**, apart from bone (heterologous), may ossify.

Clinically, the osteomata are perfectly innocent tumours. Their growth is very slow. They rarely attain a large size. They are often hereditary and multiple, in which case they usually occur in early life. Osseous growths which exhibit malignant characters are either sarcomata or chondro-sarcomata, which have undergone partial ossification. From these, true osteomata must be carefully distinguished (p. 160).

THE LYMPHOMATA.

The **Lymphomata** are new formations consisting of lymphoid, or, as it is sometimes called, adenoid tissue.

Lymphoid tissue is now known to have a much more general distribution than was formerly supposed. It not only constitutes the follicles of the lymphatic glands and the Malpighian corpuscles of the spleen, but also Peyer's glands and the solitary glands of the intestines, the follicles of the pharynx and tonsils, the thymus gland,

and the trachoma glands of the conjunctiva. More recently, lymphoid tissue has been found in other situations, as around the blood-vessels of the pia mater and of other parts, in the neighbourhood of the smallest bronchi, in the pleura immediately beneath its endothelium, in the peritoneum, in the mucous membrane of the alimentary canal, and in the medulla of bone.

Wherever it exists, the same **general structure**, that of the follicle of a lymphatic gland, may be taken as the type not only of physiological lymphoid tissue, but also of that of pathological growths. This tissue consists of a delicate reticulum, within the meshes of which are numerous lymph-corpuscles. The *reticulum* is a close network of very fine fibrils. Its meshes are only large enough to enclose one, or at most very few corpuscles in each. The fibrils usually present a more or less homogeneous appearance, and nuclei are sometimes to be distinguished at the angles of the network. The *lymph-corpuscles*, which constitute the greater part of the tissue, can in most cases be readily removed from the meshes of the reticulum by the agitation of thin sections in water. They are identical in their characters with the leucocytes of the blood. As usually seen after death, they are spheroidal, pale, semi-transparent bodies, varying considerably in size, and presenting slight differences in structure. Some are granular, and appear to possess no nucleus; in others, a distinct, simple, or compound nucleus is visible, which is usually also granular; others again are much larger, and contain two or even three nuclei (Fig. 52).

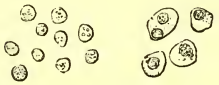


FIG. 52.—*Cells from a Lymphatic Growth in the Liver.* Those to the left are the ordinary lymph-corpuscles, which constituted the greater part of the growth. To the right are some of the larger elements. ×350.

The histological and physical characters of the lymphomata vary, according to the rapidity of their development. In the *rapidly growing forms* the proportion of cells is very great. Many of the cells are larger than those normally met with in lymphatic glands, and contain two, or even more, nuclei. The tumours are of a greyish-white colour, and soft brain-like consistence—much like encephaloid cancer—yielding abundance of milky juice. They may reach a great size. The more *slowly growing tumours*, on the other hand, are less richly cellular. The larger cell-forms are almost entirely wanting. The reticulum constitutes a more prominent part of the growth (Fig. 53) and, instead of being exceedingly delicate, is much coarser, and forms a network of broad homogeneous or slightly

fibrillated bands. As the reticulum increases, the lymph-corpuscles gradually diminish in number and become arranged in smaller groups within its meshes (Fig. 53). Such growths are much harder than the more rapidly growing ones; they are sometimes exceedingly dense, and are rarely very large. These variations in the proportion of cells and stroma are precisely analogous to those met with in lymphatic glands as the result of acute and chronic inflammation respectively; but in many cases the relation between cells and stroma remains normal, as in hyperplasia.

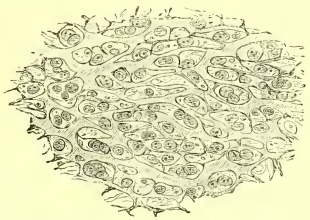


FIG. 53.—*Lymphoma*. Section of a firm lymphoma of the mediastinum. Showing a very thickened reticulum, within the meshes of which the lymphoid cells are grouped. × 200.

The lymphomata do not undergo marked **secondary changes**. There is *little tendency* to fatty degeneration, caseation, or softening, such as occurs in scrofulous glands.

The lymphomata **originate from lymphoid tissue,** being apparently uniform overgrowths of pre-existing lymphatic structures—mainly of the lymphatic glands, They are, therefore, usually homologous. They may, however, be heterologous, either owing to the new tissue extending considerably beyond the confines of its origin, or to its occurrence in situations where lymphoid tissue is not present normally. This latter condition obtains in Hodgkin's disease, and in certain forms of lymphoma which are malignant.

In some cases of round-celled sarcoma, which may originate in any onnective-tissue, the matrix undergoes development into a network; the growths spread and generalise like ordinary sarcomata, and are called **lympho-sarcomata**. They may originate in lymphatic glands.

In considering the development of these growths it must be borne in mind that enlargements of lymphatic structures are most frequently of an inflammatory nature, being due to some injury; and that histologically, as already indicated, there is but little difference between these inflammatory growths and true lymphomata. The inflammatory growths, however, tend to subside, the tumours continuously to increase. Further, the development of the tumours seems, like that of the inflammatory growths, to be occasionally determined by some injury. Thus, an injury may give rise to inflammation and enlarge-

ment of the gland; but this enlargement, instead of subsiding with the inflammation, continues to increase (see "Ætiology of Tumours").

Clinically, the lymphomata are, for the most part, perfectly innocent tumours. They originate most frequently in the lymphatic glands, which thereupon undergo a continuous increase in size. Sometimes, as already stated, the enlargement of the glands appears to be the result of injury. In most cases, however, no such source of irritation is discoverable. The glands which are especially prone to this disease are the cervical, the submaxillary, the axillary, the inguinal, the bronchial and mediastinal, and the abdominal glands. Usually only a single gland, or a single group of glands, is affected; sometimes, however, the growth is more general. As the glands enlarge, they gradually unite, so that ultimately they may form very large lobulated tumours. When occurring in the mediastinum they may invade one or both lungs: they constitute one common form of mediastinal tumour. The lymphatic structures in the intestine may in the same way become enlarged, and project, so as to form polypi.

The lymphomata occasionally exhibit malignant properties. This is especially the case in those richly cellular, soft, rapidly growing forms which are sometimes met with. Such growths may rapidly infiltrate the surrounding structures, involve the neighbouring lymphatic glands, and even infect distant parts. To these malignant forms the term **lymphadenoma** is sometimes applied.

In the condition known as "Hodgkin's Disease," and in leuchæmia, lymphomatous growths are met with in various parts of the body.

Hodgkin's Disease.

This disease is characterised by the enlargement of the lymphatic glands in various parts of the body, together with the development of lymphatic growths in internal organs, especially in the spleen, and by a progressive diminution in the number of the red corpuscles in the blood. The new growths are precisely similar, histologically, to lymphoma. The disease was first described by Hodgkin, and is called after him, "Hodgkin's Disease;" it is also known as "Anæmia Lymphatica." It is allied to leuchæmia, but differs essentially from it in this respect, that the new formation of lymphatic tissue is not associated with any notable increase in the number of the white corpuscles in the blood (see "Leuchæmia").

The lymphatic glands are usually the earliest seats of the new growth. At first only a single group of glands may be enlarged; subsequently, however, the process becomes more general, and the glands throughout the whole body may be more or less involved. The groups of glands most often affected are, in the order of their frequency, the cervical, the axillary, the inguinal, the retro-peritoneal, the bronchial, the mediastinal, and the mesenteric. The new growth, which in the earlier stages is limited to the glands, gradually breaks through the capsules, so that the enlarged glands become confluent, and form large lobulated masses. The growth may also extend still further beyond the confines of the gland and invade and infiltrate the adjacent structures.

This new growth of lymphatic tissue, which commences in and often extends beyond the confines of the lymphatic glands, is ultimately followed by the formation of lymphatic growths in various internal organs, but more especially in the spleen. The spleen is affected in a large proportion of cases. Here the new growth originates in the Malpighian bodies, and so gives rise to disseminated nodules. These vary in size from minute points to masses as large as a hazel-nut or walnut. They are usually more or less irregular in shape, of a greyish or yellowish-white colour, firmer in consistence than the splenic tissue, and not encapsuled. In addition to these, wedge-shaped infarctions surrounded by a zone of hyperæmia are sometimes met with, similar to those which are often seen in leuchæmia. The spleen itself is generally somewhat increased in size; and its capsule is usually thickened, and often adherent to adjacent organs. In quite exceptional cases the spleen is not the seat of these disseminated growths, but is simply uniformly enlarged, like the leuchæmic spleen.

The liver, kidneys, alimentary canal, medulla of bone, lungs, and subcutaneous tissue may all become involved, the new growths occurring either as nodules of various sizes scattered through the organs, or in a more infiltrated form, like many of those met with in leuchæmia.

Histologically, the new growths are precisely similar to the lymphomata, and, like these, present differences in the relative proportions of cells and stroma. The richly cellular forms are soft and pulpy, whilst those in which the stroma is more abundant are firmer and more fibrous in consistence. Retrogressive changes rarely occur.

With regard to the pathology of the disease, it is undoubtedly obscure. The development of the new growths cannot in most cases

be regarded as the result of infection from a primary centre, as the process is, for the most part, confined to the lymphatic structures, and many and widely distant groups are often simultaneously involved. The disease thus appears to occupy a different pathological position from that of the malignant tumours. It is probable that there is some special weakness of the lymphatic structures generally, which renders them prone to undergo these active developmental changes—the process being determined by some unknown factor. The progressive anæmia which accompanies, but does not precede, the gland-affection is possibly due to the progressive implication of the lymphatic structures and to the consequent interference with the formation of the blood-corpuscles. (See Leuchæmia.)

The Lymphangiomata.

The **Lymphangiomata** are tumours consisting of abnormally large lymphatic vessels. It is doubtful how much of the growth is due to simple dilatation and how much to new formation of lymphatic vessels. The divisions are the same as those of angioma—**simple** and **cavernous**. A section of the latter would scarcely be distinguishable from one of cavernous nævus (Fig. 46, p. 134), except by the contents of the spaces. There is generally fat in the stroma.

Each kind may be congenital or acquired. **Congenital** dilatations are found in the tongue (makroglossia), lip (makrocheilia), and labium, causing hypertrophy of the parts. They are also found in other parts of the skin.

Acquired dilatation of lymphatics is found in the skin, especially that of the thigh and thorax. Tumours sometimes as large as an orange may be thus formed in the subcutaneous tissue. Dangerous loss of lymph may occur from rupture of one of the vessels. Fibroid thickening may occur in the parts from which the lymphatics pass to the tumour.

CHAPTER XIV.

THE SARCOMATA.

The **Sarcomata** are tumours consisting of connective-tissue, of a more or less embryonic type, in so far, at least, that cells predominate over intercellular substance. But in central parts the process of development seems sometimes to proceed to a further stage, and fully developed connective tissues, such as fibrous tissue, cartilage or bone, are formed. In this way a mixed tumour may result.

STRUCTURE.—All sarcomata consist of cells embedded in more or less intercellular substance, which varies in amount and character, and supports the blood-vessels.

The **cells**, which usually constitute almost the whole of the growth, consist for the most part of masses of nucleated protoplasm, rarely possessing a limiting membrane. They vary much both in size and form; and though in any given tumour one form usually predominates, all may generally be found by searching *teased* preparations, which should always be employed for the purpose. Often the different forms are pretty equally mixed in the same growth. There are three principal varieties—**round, spindle,** and **myeloid** cells. The round and spindle forms may be either small or large. The irregular, multinucleated, myeloid cells vary in size, and in the number and size of the contained nuclei. One cell may have as many as thirty nuclei.

The **intercellular substance** usually exists in but small quantity. *It intervenes between all cells* and is as *closely connected with them* as in ordinary connective-tissue. These points are often relied upon to distinguish certain sarcomata from cancers; but they probably do not always hold good.

The stroma may be fluid and homogeneous, or firmer and granular, or more or less fibrous, or even chondrified and ossified. On its amount and nature the consistence of the growth depends.

The **blood-vessels** are usually very numerous, and are either in direct contact with the cells, or separated from them by a little fibrillated tissue. Their distribution is very irregular, and their walls are often formed by nothing but the cells of the tumour. Hence, on the one hand, the ease with which portions of the tumour are carried away in the blood stream and the tumour generalised; and, on the other,

the frequency with which the vessels rupture and permit extravasation of blood into the substance of the growth. Lymphatics are unknown.

An examination of the growing border usually shows a great excess of small round cells over all other forms. These cells extend along the connective-tissue in all directions, and force themselves between the essential elements of muscles, glands, and any adjacent organs, while these elements themselves become pale, undergo atrophy, and finally disappear. In the invaded connective-tissue many cell-forms are seen which may possibly indicate multiplication of the fixed cells; but it is almost impossible to obtain any proof that they help to form the tumour (see "Modes of Spread of Inflammation").

In an ordinary examination of a sarcoma, the growing edge should be avoided, on account of the predominance in that part of small round cells over those most characteristic of the tumour.

SECONDARY CHANGES.—The most important of these is **fatty degeneration**. This always occurs to a greater or less extent in the older portions of the growth, causing either softening, or the production of cyst-like cavities. It is frequently associated with rupture of the blood-vessels and **hæmorrhage**; the latter may give rise to the formation of sanguineous cysts (p. 164). **Calcification** (Fig. 60, p. 161), **ossification** (Fig. 61, p. 161), and **mucoid degeneration** are less common. The occurrence of calcification, ossification, and pigmentation is influenced by the predisposition of the matrix from which the growth is produced—thus, calcification and ossification are more prone to occur in tumours originating in connection with bone, pigmentation in those originating from the cutis or eyeball.

VARIETIES.—Though all sarcomata possess the same general characters, they present histological and clinical differences which serve as bases for their classification.

The principal features which are thus utilised are (1) the predominant form of cell; (2) the nature of the stroma; and (3) the secondary changes to which the growths are liable.

(1) The predominant form of *cell* enables us to distinguish four groups: the **round-celled**, the **spindle-celled**, the **mixed-celled**, in which no special form predominates, and the **myeloid-celled**. Strictly speaking, this last group is a mixed-celled sarcoma, but though the myeloid cells can never be said to predominate, they are

frequently so numerous as to be the most striking objects in the field, when examined microscopically.

(2) The *stroma* may be mucous, fibrous, cartilaginous or bony; hence we may have a **myxo-sarcoma**, **fibro-sarcoma**, **chondro-sarcoma**, and **osteo-sarcoma**.

(3) Sarcomata may undergo *secondary changes*, which are justifiably described as distinct varieties, inasmuch as the peculiarities are reproduced in the secondary growths. The chief of these are: **melano-sarcoma**, characterised by the development of black pigment, and **chloroma**, a very rare form, with green pigment; **lipo-sarcoma**, in which the cells undergo fatty infiltration; and **calcifying sarcoma**, in which calcareous infiltration is marked.

PHYSICAL CHARACTERS.—Portions of sarcomata which have undergone no secondary changes are soft, semi-translucent, and greyish or pinkish-grey. These appearances are best seen near the *growing edge*, which may be very narrow. The diagnosis—even with the microscope—between a sarcoma, especially a fibro-sarcoma, and the different forms of simple connective-tissue tumours may be exceedingly difficult. This is due to the higher development of the central parts of the sarcoma towards one or other variety of fully formed connective-tissue. Degenerative processes, such as fatty metamorphosis, and especially hæmorrhage, may greatly interfere with the usual appearances: the occurrence of hæmorrhage may convert a solid tumour into a blood-cyst with a scarcely recognisable wall.

As a rule, the growing edge is ill-defined, there being no sharp line of demarcation between the tumour and the adjacent parts; but sometimes a slowly growing tumour may acquire a capsule by stretching around itself the connective-tissue of the organ in which it originates.

MODE OF GROWTH AND SEATS.—The sarcomata always spring from connective-tissue, and may occur wherever connective-tissue is present. It is doubtful whether they start from adult tissue or from some embryonic remnant. Congenital warts and pigment-spots often serve in later life as their starting-points (p. 125). The skin and subcutaneous tissue, fasciæ, periosteum, medulla, and lymphatic glands, are the commonest seats of sarcomata.

CLINICAL CHARACTERS.—The sarcomata occur most frequently in early and middle life, and are among the most malignant

of new formations. They are especially characterised by their great tendency to extend locally and to infiltrate the surrounding structures, so that they are exceedingly prone to recur *in loco* after removal. Butlin has shown that sarcomata of certain parts almost always affect lymphatic glands at an early stage—viz., sarcomata of the testis, tonsil, lymphatic glands, and some fasciæ. Those of certain other parts show no tendency to affect lymphatic glands at all; so that, on the whole, sarcomata present a contrast to cancers in this respect. Like cancers they are very liable to become generalised. The secondary growths occur most frequently in the lungs. *The dissemination is effected by means of the blood,* and is a natural result of the thinness of their vessel-walls and the immediate contact of these with the cells of the growth—conditions most favourable to the entrance of the cellular elements into the circulation. The dissemination of the sarcomata is, on this account, sometimes more rapid than that of the carcinomata. *In the carcinomata, extension in the early stage takes place by the lymphatics,* and dissemination by the blood occurs later in the disease. The *secondary* sarcomata usually resemble the *primary* growth, but in exceptional cases the several varieties may replace one another.

It has already been pointed out that the different varieties of sarcoma possess very different degrees of malignancy. As a rule, the softer and more vascular the tumour, and the less its tendency to form fully developed connective-tissue, the greater is its malignancy. The soft *round-celled,* and *large spindle-celled* varieties are thus usually much more malignant than the firmer, *small spindle-celled* growths. Many small spindle-celled tumours, after removal, never recur; whilst others recur locally several times, and ultimately reproduce themselves in distant parts. As a rule, largeness of the spindle elements, and the existence in many of them of more than one nucleus, are together evidence of special malignancy. Central sarcomata of bone are much less malignant than the subperiosteal varieties; the latter, with sarcomata of the tonsil and testis, and melanotic sarcoma of skin, being among the most malignant of tumours. The presence of a capsule limiting the growth must also be taken into account in judging of the degree of its malignancy. It must, however, be borne in mind that even in a growth distinctly encapsuled, the sarcomatous elements may invade the adjacent structures. The myeloid growths are the least malignant; they may in exceptional cases give rise to secondary growths in internal organs, but "complete" removal gives

a very good chance of non-recurrence. This sometimes occurs with growths having every appearance of malignancy.

According to Cohnheim, the very varying malignancy of sarcomatous tumours goes far in proving the necessity for that diminished physiological resistance already alluded to (p. 123).

ROUND-CELLED SARCOMATA.

This is of softer consistence than the spindle-celled growths, and from its frequent resemblance in physical characters to encephaloid, it is sometimes known as "medullary," "encephaloid," or "soft" sarcoma. Histologically, it is elementary embryonic tissue, consisting mainly of round cells embedded in a scanty and usually soft, homogeneous, or finely granular intercellular substance (Fig. 54). The cells usually resemble those met with in the most elementary embryonic tissue; less frequently they are bigger, and contain large round or oval nuclei, with bright nucleoli. There is an almost complete absence of fusiform cells, and of the partial fibrillation which is so frequent in the more highly developed spindle-celled variety.



FIG. 54.—*Round-celled Sarcoma.* A thin section of a small round-celled sarcoma of the liver. × 200.

The round-celled sarcomata are of a uniformly soft, brain-like consistence, somewhat translucent or opaque, and of a greyish or reddish-white colour. On scraping the cut surface, they yield a juice which is rich in cells. They are exceedingly vascular, the vessels often being dilated and varicose, and, from their liability to rupture, they frequently give rise to ecchymoses and to the formation of sanguineous cysts (see "Blood-Cysts"). They grow from the cutis, the subcutaneous cellular tissue, the periosteum, the fasciæ, and the connective-tissue of organs. They extend rapidly by peripheral growth, infiltrate the surrounding structures, reproduce themselves in internal organs, and often involve the lymphatic glands. From their clinical and physical characters, these tumours are very liable to be confounded with encephaloid cancer—they are distinguished by the absence of an alveolar stroma, and by the penetration of the intercellular substance between the individual cells.

GLIOMA.—This is a variety of round-celled sarcoma growing from

the neuroglia or connective-tissue of nerve. It consists of very small round cells, embedded in an exceedingly scanty, homogeneous, granular, or slightly fibrillated intercellular substance (Fig. 55). Some of the cells may possess fine prolongations which, by communicating with one another, form a somewhat reticulated structure. These tumours are of soft consistence, and of pinkish-grey colour.

Gliomata occur in the grey and white substance of the brain, in the cranial nerves, and in the retina. In the retina a glioma usually com-

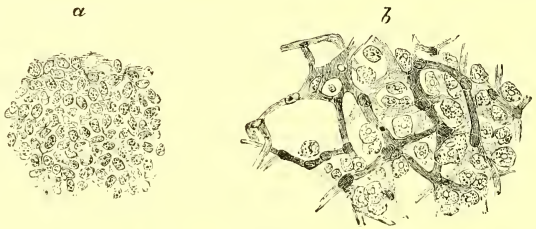


FIG. 55.—*Sarcomatous Tumours from the Brain.* *a*. A glioma of the cerebellum, showing the appearance ordinarily presented by these growths. *b*. A comparatively rare form of sarcoma, consisting of large nucleated cells enclosed within the meshes of a vascular network. The development of this tumour took place in the brain subsequently to that of spindle-celled growths—primarily in the thigh, and secondarily in the lung. × 200.

mences as a minute nodule, which may gradually increase until it projects as a large fungating tumour from the orbit. Although gliomata grow slowly, they are not encapsuled; and although they may occasionally infiltrate the tissues in which they lie and cause secondary growths in their immediate vicinity, they very rarely reproduce themselves in neighbouring lymphatic glands or in distant organs. They are liable to small hæmorrhages into their structure, and sometimes become more or less caseous. So often are these growths clinically "innocent," that by some they are classed as a variety of connective-tissue tumour, of a "neuroglia" type, which may occasionally become sarcomatous.

LYMPHO-SARCOMA.—This is a round-celled sarcoma, in which the matrix has developed into a more or less perfect reticulum, like that of lymphoid tissue. It may begin in lymphatic glands, or in connective-tissue anywhere. It is distinguished from lymphoma by its more rapid course, and by the formation of secondary growths by embolism (p. 151).

ALVEOLAR SARCOMA.—This is a rare form of round-celled sarcoma which was first described by Billroth. The cells, which are large, sharply defined, round or oval in shape, and contain round, prominent nuclei, are separated from each other by a more or less marked fibrous stroma. In some parts this stroma forms small alveoli within which the cells are grouped; but careful examination will always show that in most parts of the section the stroma really penetrates between the individual cells. This last named character, together with the nature of the tissue from which they arise, serves to distinguish these tumours from the cancers, with which, in many cases, they may easily be confounded. The accompaning drawing shows their microscopic characters (Fig. 56). The stroma is often much more delicate, and the cell-masses are occasionally much larger than in the drawing. The cells are generally in close connection with the stroma, though vessels never pass in among them. In this latter respect they resemble epithelial growths. Ziegler says the alveolar structure may be due to the transformation of normal intervascular tissue into sarcoma-cells, whilst the vessels with the neighbouring connective-tissue remain as septa.

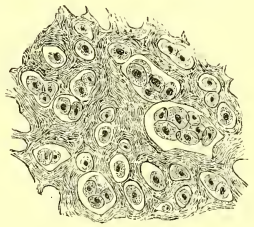


FIG. 56.—*Alveolar Sarcoma.* From a tumour of the Skin. × 200. (Godlee.)

Alveolar sarcomata are met with principally in the skin, bones, and muscles. In the skin, where they are often multiple, they lead to ulceration. They tend to recur locally, and also to reproduce themselves in internal organs.

SPINDLE-CELLED SARCOMATA.

These tumours, which include the growths described by Paget in this country as "fibro-plastic," and "recurrent fibroid," are the most common of all the sarcomata. They consist of cells, mainly spindle-shaped and fusiform, separated by only a little homogeneous or slightly fibrillated intercellular substance, and often forming whorls round the vessels. The cells contain well-marked oval nuclei, with one or more nucleoli. They are arranged in bundles which pass in all directions through the growth, and often give it the appearance of a fibroma or myoma. In those portions of the section in which the bundles of spindle elements have been cut transversely, or obliquely,

they present the appearance of round or oval cells. The cells vary considerably in size in different tumours, hence the division into **small** and **large** spindle-celled growths.

SMALL SPINDLE-CELLED SARCOMA.—In these the cells are small, often not more than $\frac{1}{1500}$ inch in length, and the intercellular substance is occasionally imperfectly fibrillated (Fig. 57). These growths approach therefore the confines of the fibromata, and histologically they must be regarded as occupying an intermediate place between embryonic and fully developed connective-tissue. They grow from periosteum, fasciæ, and connective-tissue in other parts. They are usually firm and whitish or pinkish-white, and present on section a translucent somewhat fibrillated appearance. They are much more frequently encapsuled than any other variety of sarcoma, but they are very liable to infiltrate the surrounding structures, and to recur locally after removal.

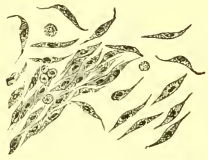


FIG. 57.—*Small Spindle-celled Sarcoma.* From a tumour of the leg. × 200.

LARGE SPINDLE-CELLED SARCOMA.—The cellular elements in these tumours are much larger than in the preceding.

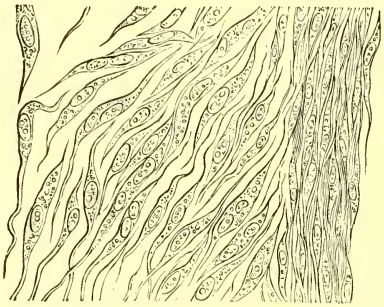


FIG. 58.—*Large Spindle-celled Sarcoma.* To the left—the cells have been separated by teasing, so that their individual forms are apparent; to the right—they are in their natural state of apposition, such as would be seen in a thin section of the tumour. (Virchow.)

The cells are plumper, and both nuclei and nucleoli are especially prominent, and frequently multiple (Fig. 58). The intercellular substance is more scanty, and there is a complete absence of any

fibrillation. These growths are much softer in consistence than the small-celled variety. They are of a pinkish-white colour, and are often stained by extravasations of blood, and in parts are sometimes almost diffluent from extensive fatty degeneration. They grow rapidly, and are usually exceedingly malignant.

MELANOTIC SARCOMA.—This is a variety of sarcoma in which many of the cells contain granules of dark-coloured pigment,

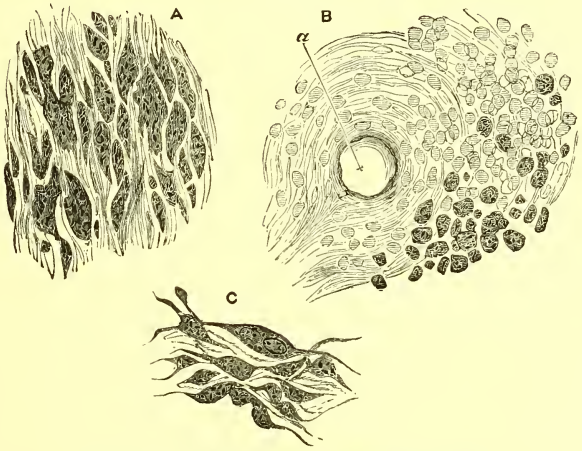


FIG. 59.—*A Melanotic Sarcoma of the Penis.*

A. Section showing the general arrangement of the elements. × 200.

B. Section from the peripheral part of the growth, showing the "indifferent cells," amongst which are small isolated pigmented elements. At *a*, a blood-vessel is seen. × 200.

C. Some of the elements separated by teasing. In these the pigment-granules are well seen. × 400.

quite distinct from the pigment of extravasated blood. By far the greater number of melanotic tumours are sarcomata, and most of the growths, which were formerly described as "melanotic cancers," belong in reality to this class of new formations.

The melanotic sarcomata originate principally in two situations—in the choroid coat of the eye, and in the superficial integuments. In both of these situations pigment is a normal constituent of the tissues, and this tendency of pigmented structures to originate melanotic growths is exceedingly characteristic. These tumours usually consist of spindle-shaped cells (Fig. 59), and hence they are described in the

present section; but in some cases the prevailing type of cell is round or oval. The pigment, which gives to them their distinctive characters, consists of granules of a brownish or dark sepia colour. These are mainly distributed within the cells (Fig. 59, c), but are also found in the intercellular substance. Frequently, only a very small proportion of the cells are pigmented, whilst in other instances the pigmentation is much more universal. In all cases, a large number of the elements will be found to be quite free from pigment.

These melanotic tumours are amongst the most malignant of the sarcomatous growths. Although they show comparatively little tendency to extend locally, they are rapidly disseminated by means of the blood-vessels, and occasionally also by the lymphatics: they thus reproduce themselves, often very rapidly, in distant tissues. Although the secondary growths almost invariably maintain their melanotic character, the degree of their pigmentation varies considerably. Whilst many of them may be perfectly black in colour, others may be much paler—perhaps only streaked with pigment. The secondary growths are soft, usually distinctly circumscribed, and often encapsuled. They may occur in almost every organ of the body—the liver, the spleen, the kidneys, the lungs, the heart, the brain and spinal cord, and also the lymphatic glands and subcutaneous tissue, may all be simultaneously involved. When occurring in internal organs, the pigmentation is not always limited to the secondary nodules, but many of the cells proper to the organ itself are filled with granules of similar pigment, which is most abundant in the cells immediately adjacent to the new growth. This pigmentation of the cells of the organ often extends for some distance beyond the confines of the tumour.

OSTEOID SARCOMA.—This is a variety of sarcoma which was formerly known as "osteoid cancer." The growth (usually spindle-celled) is either more or less calcified, or partially converted into true bone. As a primary growth it is met with almost exclusively in connection with bone, growing either from the periosteum or the medulla; but the osteoid characters are usually reproduced in secondary tumours occurring in the lungs and other parts.

Calcification is much more common than true *ossification*. Each of these processes may occur separately, but they are often combined. Bands and patches of granular appearance, in which the outlines of cells may still be visible, or in which all structure has disappeared, and which stain but slightly, show where calcification has occurred

(Fig. 60). In other parts, especially near the bone, spicules having the structure of more or less perfect bone—Haversian canals, lacunæ, and

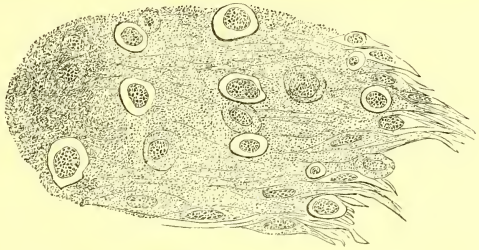


FIG. 60.—*Calcifying Sarcoma.* From a secondary tumour of the lung. Showing the calcification of a spindle-celled growth, and the formation of broad bands of calcified intercellular material enclosing spaces which contain round and oval cells. × 200.

imperfect canaliculi—will be seen penetrating the growth (Fig. 61). The spicules are generally vertical to the surface of the bone. In some



FIG. 61.—*Ossifying Sarcoma of Lower Jaw.* *s.* Sarcoma-tissue; *b.* new bone, growing from jaw, of which the structure is fairly typical; *p.* point of commencing ossification. Only nuclei of cells are indicated; close to the bone the stroma is very fibrous. × 40. (Boyd.)

cases a skeleton of bony spines radiates from the bone through the growth.

Both calcification and ossification may be very complete, but *a thin*

margin of sarcoma-tissue is always present. A simple osteoma would have cartilage or periosteum on its surface and would be of much slower growth. It is most important to recognise this difference.

MYELOID SARCOMA.

This, which is the well-known "myeloid tumour," is somewhat allied to the spindle-celled growths. It possesses, however, certain histological peculiarities which probably depend upon the characters



FIG. 62.—*Myeloid Sarcoma.* (Virchow.)

of the tissue from which it grows. Myeloid tumours nearly always occur in connection with bone, and most frequently originate in the medullary cavity. They contain many of the large, multi-nucleated cells, already described as "myeloid cells"—which resemble the cells of the medulla in a state of excessive nutritive activity—together with numerous fusiform cells like those met with in the spindle-celled varieties. There are also some smaller round and oval elements. The large myeloid cells which give to these tumours their distinctive characters, are usually much more numerous in those growths which originate in the medullary cavity than in those which spring from the periosteum. These various forms of cells are almost in contact, there being very little intercellular substance (Fig. 62). The growths are

sometimes so vascular as to give rise to distinct pulsation. They often contain cysts.

Myeloid tumours almost always grow in connection with bone, the ends of the long bones being their favourite seat. They are also frequently met with springing from the periosteum of the upper and lower alveolar processes, where they constitute one form of **epulis.** When originating within the medullary cavity, the compact tissue of the bone becomes "expanded" over them, and they thus often communicate to the fingers, during examination, the peculiar sensation known to surgeons as "eggshell crackling." True expansion of bone is, of course, impossible—really, the old bone is absorbed from within by the tumour, and the periosteum lays down new bone on the surface; absorption is more rapid than new formation, and the thin surface layer of bone yields and crackles under pressure, or is actually wanting at spots where pulsation is marked.

These tumours are for the most part of firmer consistence than the other varieties of sarcoma. Many of them are firm and fleshy; others are softer, more resembling gelatin-size. They are not pulpy and grumous like the soft sarcomata, neither do they present the fasciculated appearance of the spindle-celled varieties. Their cut surface has a uniform succulent appearance, often mottled with patches of red. This red-brown or maroon colour varies with the number of giant-cells present, and is very characteristic. The tumours are often encapsuled by the periosteal covering of the bone from which they grow. They are rare after middle life, and are the least malignant of all the sarcomata.

Cylindroma.

The name **Cylindroma** is applied to a group of tumours in which the cells are arranged in hollow columns or globes. The interior of these structures is frequently, but by no means always, occupied by a blood-vessel surrounded by hyaline material. According to some authorities, these tumours are really **myxo-sarcomata** from the first. In the opinion of others, they are sarcomata in which the adventitia of the vessels has undergone mucoid degeneration, while the vessels themselves have developed varicose dilatations. Ziegler, to emphasize the large size and number of the vessels, and the general character of the tissue around them, has suggested the name **angio-sarcoma myxomatodes.** In all probability several forms of new growth have been included under the name cylindroma.

Blood-cysts.

Tumours are occasionally met with, into which so much hæmorrhage has taken place, that their real nature is masked, and their appearance is that of blood-cysts. The nature of these blood-cysts has only recently been understood. They are now known to be in the majority of cases soft, round or spindle-celled sarcomata. They consist of broken-down blood-coagula surrounded by an ill-defined layer of soft sarcoma-tissue, which is, as a rule, clearly revealed by the microscope. These growths are exceedingly malignant, and hence the recognition of their sarcomatous origin is all-important.

CHAPTER XV.

EPITHELIAL TUMOURS.

THE PAPILLOMATA.

The **Papillomata** are new formations resembling in **structure** ordinary papillæ.

They consist of a basis of connective-tissue, which sends towards the surface numerous papillary processes, each supporting blood-vessels which end in a capillary network or single loop, the whole being enveloped in a covering of epithelium. The papillæ may be short and simple as in an ordinary wart; or they may be long, delicate, branching —giving off secondary and tertiary offsets—and very numerous, as in *villous tumours*. The covering epithelium in skin-growths is thick, hard and stratified, and may actually bind the papillæ into a solid mass; but on mucous membranes the slender vascular processes are covered by a small amount of delicate epithelium, and in consequence they are easily lacerable. Warts on serous membranes are often covered by a *single* layer of endothelial cells.

Hæmorrhage and ulceration resulting from injury can hardly be classed as **secondary changes**. The only important change is the possible conversion of a papilloma into an epithelioma. In a wart all the epithelium is *on the surface*—no matter how irregular that surface may be. As soon as the epithelium begins to *invade the tissues beneath it*, the wart has become a cancer. Pigmented warts not uncommonly

form on the face in old age, and it is well to watch but *not* to irritate them.

Four **varieties** can be readily distinguished.

1. The **ordinary skin-wart** with its covering of hard squamous epidermis. Condylomata and venereal warts, due to the irritation of the secretions of soft sores or gonorrhœa, deserve special mention. These, though covered by squamous epithelium, are much softer, more

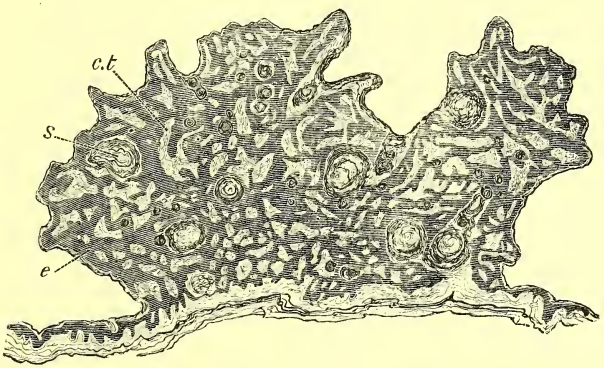


FIG. 63.—*Section of Wart on Skin of Abdomen.* *e.* Epithelium; *c.t.* connective-tissue continuous with epidermis and cutis; *s.* accumulations of horny epidermis deep down between the papillæ, looking in section like large nests. × 10. (Boyd.)

vascular, and more luxuriant in growth than the ordinary skin-wart. They affect warm, moist parts.

2. The **soft warts** and villous tumours of all mucous surfaces. These are usually characterised by long delicate compound papillæ. The tongue, cheek, larynx, and bladder are the parts most often affected. The papillary enlargements of the synovial villi, which are common in chronic arthritis, may be included in this group.

3. **Corns.**—These *commence* as papillomata; but, as the epidermis thickens and is pressed by the boot into the soft parts, the papillæ ultimately atrophy.

4. **Horns** some inches long occasionally springing from the skin. These consist of epithelium and sebaceous secretion, and originate from sebaceous follicles or from a sebaceous cyst. It is said that long papillæ project into their bases, so they seem to be allied to warts. The base must be removed with the horn, or the latter will recur.

To the **naked eye** the ordinary wart is a hard, abruptly elevated

little mass, apparently formed of epithelium. It presents an irregular ("warty") surface often divided by deep fissures. If the investing epithelium be abundant, or the papillæ be very short, a rounded mass having a merely furrowed surface results; but as the papillæ lengthen and the epithelium thins, the growth presents first a cauliflower, then a branched, and finally a villous appearance. The latter appearance is best seen on placing a "villous tumour" of the bladder in water, when the long delicate papillæ float up. They are exceedingly vascular. On section of a papilloma the relation between stroma and epithelium, above described, can be seen, even with the naked eye (Fig. 63).

Papillomata always **originate from skin,** or from mucous, serous, or synovial membranes. They most frequently grow from pre-existing papillæ; sometimes, however, they occur where no papillæ exist, springing directly from the sub-epithelial connective-tissue—this is the case in the stomach and larynx. As all new growths on free surfaces tend to become "papillary," this form of tumour is probably the result of physical conditions. According to this view a wart is simply a fibroma become papillary by an accident of position; and papillomata as a class should therefore disappear.

Clinically, warts, so long as they remain warts, are quite innocent. They are common in childhood and early adult age, especially upon the hands and face. They may be single, but upon the hands they are commonly multiple. They generally disappear after a time, though they may persist for years. Warts on mucous surfaces give trouble, and may cause death by bleeding: in the bladder, difficulty may arise from obstruction to the inflow or outflow of urine, the entrance of the ureter being a favourite seat. Lastly, the tendency of warts and warty surfaces (*ichthyosis linguæ*) to become epitheliomatous in advanced life must be remembered.

THE ADENOMATA.

The **Adenomata**—or, as they are more commonly called, **glandular tumours**—are new formations of gland-tissue, more or less atypical in structure, having an abnormal relation to the tissue around, and incapable of performing the function of the gland they imitate. Their ducts do not enter those of the gland whence they spring.

In **structure** the adenomata resemble either the racemose or tubular glands, and are divided into two corresponding **varieties**.

1. The **racemose adenomata** consist of numerous saccules or acini,

lined with small epithelial cells. These usually form a single layer, though they may be two or three deep. A section cut very obliquely through the wall of one of these acini will, by cutting across adjacent cells at different levels, give the appearance of superimposed layers. The acini communicate with each other and are grouped together, being separated merely by connective-tissue, in which are contained the blood-vessels. The connective-tissue varies in amount; when much in excess

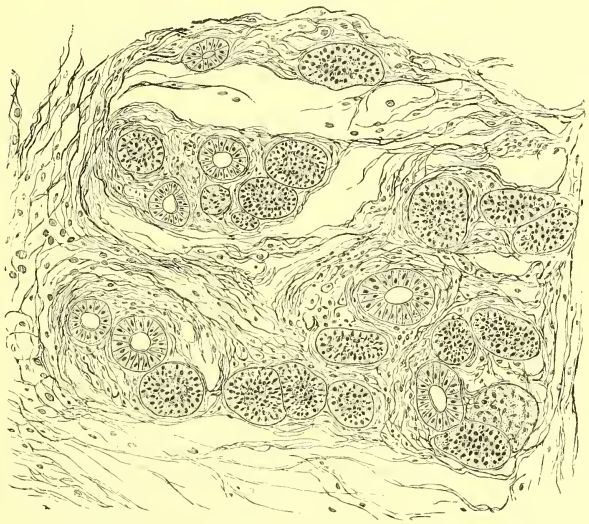


FIG. 64.—*Adenoma of Mamma.* × 200. Reduced ½. (Cantlie.)

of the normal, the growth is called an **adeno-fibroma**. Sometimes, in the most rapidly growing forms, the stroma is richly cellular, consisting of round and spindle elements: the histological distinction between such growths and sarcomata is impossible (Fig. 64).

All growths originating in glandular organs may be associated with more or less glandular structure. In the mamma, for example, sarcoma, myxoma, and other forms of tumour, are often so intermingled with the gland-tissue of the organ that it becomes difficult to say which is the predominant structure. In many cases it is evident that the development of such tumours is accompanied by an increase of the gland-tissue amongst which they grow. Mixed forms are thus produced—**adeno-sarcoma, adeno-myxoma**, &c. Adenoma is, by itself, an insufficient

name for these tumours, because their stroma is different from, or in excess of, that found in normal gland-tissue.

2. The **tubular adenomata** grow from mucous membranes, and consist of groups of tubules lined with epithelium. They will be alluded to hereafter.

The adenomata almost always **originate from pre-existing glands.** They generally grow slowly, and possibly from some hitherto



FIG. 65.—*Adeno-Fibroma of Mamma.* Showing new growth of gland structure and of connective-tissue. × 100. Reduced ½.

quiescent congenitally misplaced rudiment; otherwise it is difficult to explain the complete encapsulation and separation from the normal gland which distinguish an adenoma from a localised enlargement. The latter swelling remains in intimate relation with the gland, and is probably often of inflammatory origin.

The most frequent **secondary change** found in these tumours is **fatty degeneration** of the epithelium, which may give rise to the formation of small caseous masses in the growth. Dilatation of the saccules and tubules into **cysts,** and **mucoid softening** are also common. The origin of cancer has several times been traced to an adenoma.

The word adenoma has been used loosely, as already pointed out, to include all new formations of gland-tissue.

Adenomata occur in the following organs:—

Mamma.—This is much the most common seat of adenoma, or rather of adeno-fibroma; for a glandular tumour which is structurally indistinguishable from normal breast is very rare (Fig. 64). The arrangement of the epithelium, the number and size of the spaces, the proportion of stroma, and the number of cells it contains, is more or less abnormal (Fig. 65), hence the name adeno-fibroma is generally most applicable. These tumours are also called "Chronic Mammary" and "Adenoid." They are encapsuled, are round, oval, or lobulated, and lie in or on the breast. They are of hard elastic consistence. Their section is convex rather than cupped. It is either lobulated and fibrous-looking, or shows distinct slits and a racemose structure even to the naked eye. These tumours are most common in early life. They may be multiple. Many adeno-fibromata contain cysts, which may be very numerous, and vary in size from slight dilatations of ducts and acini to cavities holding some ounces. These cysts contain yellow, mucoid fluid, which may be reddish or brownish from extravasated blood. Many are lined with cylindrical epithelium like that of the gland spaces; but others appear to be formed by localised softenings of the stroma. At first they appear on section like irregular and branched fissures, then like spaces full of fluid: in other cases they are almost completely filled by papillary fibrous growths projecting inwards from the wall and covered by cubical epithelium. These cystic growths are called **cystic adenomata**; or, if the stroma is richly cellular, **cystic adeno-sarcomata.**

The non-cystic growths must be distinguished from local and general hypertrophies of the gland.

Ovary.—Many compound ovarian cysts are really cystic tubular adenomata, and often contain papillary growths (Fig. 66).

Testis.—No pure adenomata occur, but only mixed tumours, like those in the parotid gland.

Prostate.—In advanced age some of the tumours which form in this body contain glands as well as muscle and connective-tissue (Adeno-myoma).

Thyroid.—Apart from the hypertrophy of endemic goître and Graves's disease, distinct encapsuled tumours having the structure of the normal thyroid may occur in the substance of that gland.

Parotid.—Pure glandular tumours are infrequent, and the gland-

epithelium of such tumours as do occur is generally very atypical. Fibro-adenomata are commoner. The *ordinary* "parotid tumour" is "mixed," containing cartilage, mucous and other tissues. The other salivary glands are still less frequently affected.

Liver.—Small encapsuled tumours having the structure of the liver have been described.

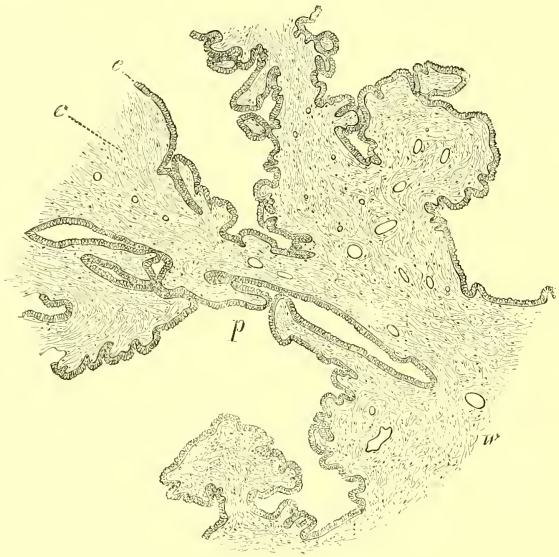


FIG. 66.—*Papillary Growth inside an Ovarian Cyst*, projecting from its wall (*w*). It consists of loose connective-tissue (*c*), containing many branched cells, covered by a layer of columnar cells (*e*). Secondary processes are numerous (*p*). × 40. Reduced ½. (Boyd.)

Glands of Mucous Membranes.—Gland-tissue enters largely into the structure of some of the "mucous" polypi which may spring from any mucous membrane, especially in catarrhal states. In some cases it is probable that the glands primarily enlarge, then project, and finally become polypoid. In other cases it is supposed that localised increase of connective-tissue from inflammation may lead to increase of the epithelial structures in relation with it. Polypi of the nose, stomach, intestines, rectum, and uterus are examples. The connective-tissue is soft and œdematous; the surface is covered by the epithelium of the part.

Sebaceous and Sweat Glands.—So-called adenomata of these

glands are uniform enlargements rather than tumours. Fig. 67 shows a small portion of a sebaceous "adenoma" from the chin of a child.

Among **secondary changes** are **calcification**, which may affect the epithelial masses, and **ossification**, which may take place in the fibrous stroma. Tumours undergoing the latter change are rare, and have been called "osteomata" of the skin (p. 145).

Adenomata afford further support to Cohnheim's view concerning the nature of malignancy (p. 123). Adenomata and adeno-fibromata

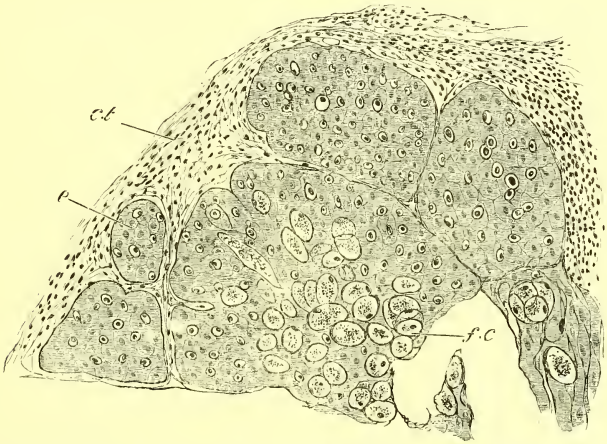


FIG. 67.—*Lobule of a Sebaceous Adenoma.* *c.t.* Connective-tissue containing many cells, and forming capsule and septa. *e.* Saccule full of epithelial cells, few of which show signs of fatty degeneration—a clear space, pushing nucleus aside. In larger saccules degeneration is more general and extreme (*f.c.*). × 200. (Boyd.)

are almost invariably innocent. Occasionally, cases occur which clinically and microscopically appear to be ordinary adenomata, but which recur locally after removal. It is no explanation to call these sarcomata. Again, there are several cases on record of the generalisation of ovarian adenomata as well as of tumours having the structure of the normal thyroid gland.

The lumina of racemose adenomata are sometimes filled up with epithelial cells; it is then impossible to distinguish them microscopically from scirrhus in its earliest stage—that of multiplication of epithelium. Indeed, the origin of cancer from adenomata has been proved several times—both microscopically and clinically.

As sarcoma-tissue passes insensibly into fibrous, it is often impossible to say with certainty which name—adeno-fibroma or adeno-sarcoma—should be applied to a given tumour containing gland-tissue.

THE CARCINOMATA.

The **Carcinomata** or Cancers are, of all new formations, the most atypical. They are made up of cells of the epithelial type, grouped irregularly in the alveoli of a more or less dense fibroid stroma. The "epithelial type" implies origin from epiblast or hypoblast, and the absence of intercellular substance; it does not imply any specific form of cell.

The alveolar structure, as seen in sections, has caused it to be said that cancer is an atypical gland-structure. Every tumour is atypical morphologically and physiologically; almost all are so structurally. In cancer we have epithelial cells, often of the most abnormal form, filling up the lumina of gland tubes (if it start from a gland), bursting through their basement or limiting membrane, and ramifying in the spaces of connective-tissue. The only type for such a process as this is the development of a gland (like the liver) by the growth of solid hypoblastic rods into a mesoblastic stroma.

STRUCTURE.—In dealing with the **microscopic structure**, we have to describe, first, the epithelial cells; and, secondly, the stroma which forms the spaces in which they lie.

The **cells** are characterised by their large size, by the diversity of their forms, and by the magnitude and prominence of their nuclei and nucleoli (Fig. 68). They are round, oval, fusiform, caudate, or polygonal—exhibiting, in short, every diversity of outline. These variations in form are principally owing to the mutual pressure to which, in their growth, they are subjected. The nuclei are large and prominent, round or oval in shape, and contain one or more bright nucleoli. The nuclei are, perhaps, most frequently single, but two are often met with, and in the softer and more rapidly growing cancers there may be more. The cells lie loosely in the alveoli, and *no* stroma passes between them. They rapidly undergo retrogressive changes; hence they usually con-



FIG. 68. — *Cells from a Scirrhus of the Mamma.* × 350.

tain molecular fat. Sometimes so many have been destroyed that more free nuclei are visible than cells. Cells precisely similar to these are met with in other morbid growths, and also in the normal tissues. There is thus no *specific* "cancer-cell."

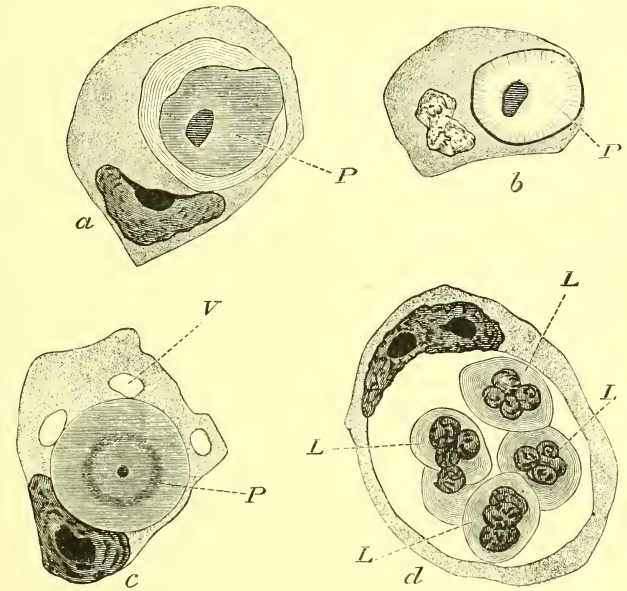


FIG. 69.—*Cancer-cells containing "Cancer-bodies."*

(*a*) Cancer of Stomach. Cell from secondary nodule in liver. Nucleus of cell is near *a*. Nucleated parasite is in the centre (*P*). × 1200.

(*b*) Cancer-cell from scirrhus of breast. Faint rays are seen at periphery of parasite (*P*). × 1200.

(*c*) Cell from same specimen as (*a*). Three vacuoles (*V*) are seen round upper half of parasite (*P*), nucleus of which is very small. The nucleus occupies the lowest part of the cell. × 1200.

(*d*) Cancer-cell containing four multinucleated leucocytes (*L*) which have destroyed the parasite. × 1200.

(Specimen and drawing by Dr. Ruffer.)

During the last few years the minute structure of cancers has been subjected to a very rigid examination in search for any parasite that may be present. Nearly all observers are agreed that, when suitable portions of cancerous tissues are hardened and stained by special methods, peculiar appearances, the significance of which is still in dispute, are to be seen. These are known as "cancer-bodies" or "cell-

enclosures." They vary greatly in size, being on an average somewhat smaller than red corpuscles. They are encapsuled, and for the most part, spheroidal: they have a sharply defined outline. They possess staining affinities somewhat different to those of the ordinary cells of the growth. Their protoplasm is usually homogeneous, but occasionally mottled or granular. At or near their centre is a small deeply stained part, which in all probability is a nucleus or nucleolus. This so-called nucleus is generally round or oval. There is usually but one, and this

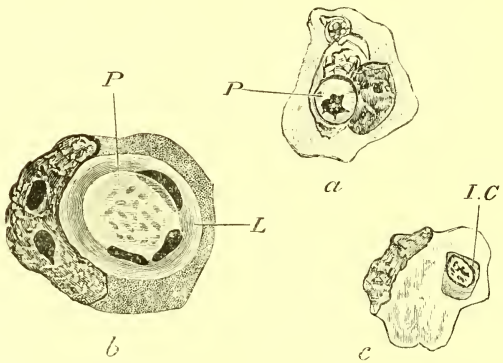


FIG. 70.—*Cancer-Cells.*

(*a*) Parasite (*P*) by the side of the cell nucleus. × 600.

(*b*) Cancer-cell containing a parasite (*P*) enveloped by a multinucleated leucocyte (*L*). The nucleus of the cancer-cell is on the left. × 1200.

(*c*) Cancer-cell showing part of an invaginated cell (*I.C*) simulating a parasite. × 600.

(Specimen and drawing by Dr. Ruffer.)

may be connected with the periphery by faint rays (Figs. 69 *b*, and 70 *a*). The cancer-bodies commonly multiply by binary division: the occurrence of sporulation, although affirmed by some, is denied by most. They are usually found enclosed in the ordinary cells of the growth, but they have been described in the alveolar spaces outside the cells, and even in the lymphatics of the alveolar walls. Their position has no ascertainable influence on their general characters. As a rule, no cancer-cell contains more than one of them. The cancer-body may occupy only an insignificant part, or it may fill nearly the whole of the cell, and displace the nucleus to the periphery. Still more rarely these bodies may be found, singly or in numbers, in the nucleus itself: in this case they are generally smaller than when found elsewhere.

The cancer-bodies are most common in growing edges and in secondary deposits, and are rarely, if ever, found in degenerated parts. On the other hand, there is no evidence that they excite any unusual activity of growth in the cells containing them. As they degenerate, they lose their sharp contour; and Ruffer has drawn attention to the fact that this not infrequently happens when a leucocyte invades a

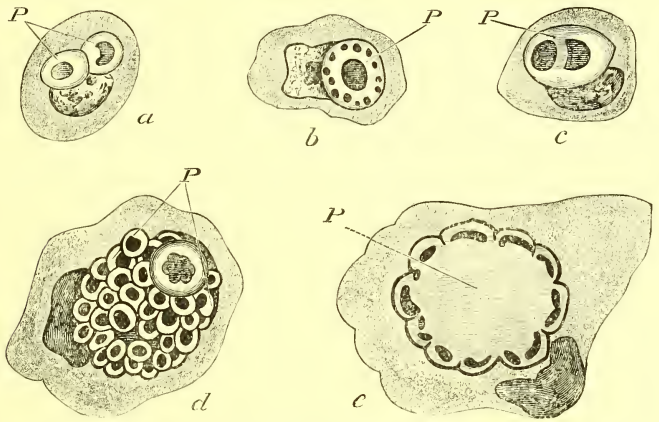


FIG. 71.—*Cancer-bodies showing probable methods of reproduction.*

(*c*) Nucleus of parasite is dividing, and the connecting threads are shown. × 600.

(*a*) Division of nucleus and cell-wall is complete. × 600.

(*b*) Parasite showing granules at the periphery of the cell. × 600.

(*e*) Commencing segmentation of parasite, showing a scalloped margin, each segment of which contains a portion of the fragmented nucleus. × 1000.

(*d*) Cell containing a cluster of small parasites, presumably a later stage of the process seen in (*e*). × 1000.

Compare these with drawing of malarial parasites. (Specimen and drawing by Dr. Ruffer.)

cancer-cell already occupied by one of these "cancer-bodies." The nature of these bodies is discussed on p. 178.

The **stroma** varies considerably in amount, being much more abundant in some specimens than in others. It consists of a more or less distinctly fibrillated tissue arranged so as to form alveoli of various shapes and sizes, within which the cells are grouped (Figs. 72 and 74). It is not closely connected with the cells and none penetrates between them. These alveoli communicate with one another, so as to form a continuous cavernous system. The characters of the stroma

vary with its rate of growth—if this is rapid, it will contain some round and spindle-shaped cells (see Figs. 76 and 81); if, on the other hand, it is slow, or has altogether ceased, the tissue will contain few or no cells, and will be denser and more fibrous in character (Fig. 74). The latter is the condition in which it is most commonly met with.

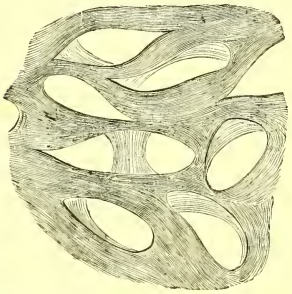


FIG. 72.—*The Alveolar Stroma from a Scirrhus of the Mamma.* The cells have been removed by pencilling. × 200.

In the stroma are the **blood-vessels.** These are often very numerous, and form a close network round the alveoli. They are limited to the stroma, and never pass into the epithelial masses. This distribution of the blood-vessels is important, as it serves to distinguish the carcinomata from the sarcomata (p. 151). To alveolar sarcomata and tumours springing from endothelium, this rule, however, does not apply.

Lymphatics communicate freely with the alveoli. This explains the great tendency of cancer to infect the lymphatic glands. In fact, the alveoli may be regarded as dilated lymphatics, for the epithelial columns grow along lymphatic spaces—the lines of least resistance.

ORIGIN.—The question of the **genesis of carcinoma** involves that of the genesis of epithelium generally. It is maintained by most histologists that epithelium can originate only from epithelium, and that the epiblast and hypoblast are the sources from which all epithelium is subsequently derived. Others state that epithelium may originate also from connective-tissue. A like difference of opinion exists as to the source of the epithelioid cells of cancer. By many they are regarded as originating only from pre-existing epithelium. Others maintain that they may be derived also from cells belonging to the connective-tissue. It is also believed by some that many cancers originate from the endothelium of the lymphatics—*i.e.*, specialised connective-tissue corpuscles.

Nearly all modern observations tend to support the epithelial origin. This renders it impossible for true cancer to arise in any mesoblastic structure. Cases have been reported of primary cancer in lymphatic glands, in bone, in the membranes of the brain, and in other places. Of these cases there are three possible explanations: (1) some small primary growth, which gave rise to no symptoms, may

have been overlooked; (2) some abnormality may have existed, such as a detached piece of mamma lying near the axillary glands, or the fœtal inclusion of an epithelial rudiment; (3) the growth may have been one of those sarcomata which can be distinguished from true cancer only by the closest examination, and by careful inquiry into their development (alveolar sarcomata, cylindromata).

Epithelial cells are said to occur round a cancer, quite isolated from it. They lie in the connective-tissue spaces. The isolation is very difficult to prove, and does not necessitate the origin of the cells from connective-tissue elements, for the cells may have been carried by the lymph-stream, aided by the spontaneous movements noted in cancer-cells by Carmalt. Often delicate chains of cells one to two inches long have been traced between a main growth and an apparently isolated nodule—such a chain might easily be interrupted. It is worthy of note that very few cases of so-called primary mesoblastic cancer are *now* reported.

It is most probable, therefore, that a cancer originates either in the growth of a resting embryonic epithelial rudiment (Cohnheim), or in the multiplication of some epithelial cells. Other conditions being favourable (p. 123), the cells grow through any basement membrane that may exist, and spread in the connective-tissue along lymph-spaces and channels. At this stage the epithelial cells actually lie in the lymph-current, where they would naturally multiply very rapidly, being bathed in nutrient fluid. In this way glandular infection is easy to explain. Where resistance is great the growing cell-columns are narrow; where it is slight they widen out.

The connective-tissue bundles of the part are at first the only constituents of the stroma, but round-celled infiltration, probably the result of more or less intense inflammation excited by the epithelial invasion, soon appears, and is followed by fibroid tissue which contracts. At first, other elements of the part may also persist in the stroma—*e.g.*, fat-cells in the breast, and muscle-fibres in the prostate.

With this mode of growth, the carcinomata never become encapsuled, but gradually infiltrate surrounding structures. This process of infiltration is very characteristic, and is more marked in cancer than in any of the malignant growths. A zone of small-celled infiltration is seen for some distance around the confines of the tumour, so that there is no line of demarcation between it and the normal structures (Fig. 73).

There is at present no general agreement concerning the nature of the "cancer-bodies," before described, or the part they take in the origin and growth of cancer. Ruffer compares them to the protozoa of malaria (see "Malaria"); and by many observers they are thought to be parasitic. The evidence in favour of this view may be thus summarised :—(1) their occurrence within the cell as a distinctly foreign substance; (2) their appearance, so strongly suggestive of an organised structure; (3) their staining reactions, so distinct from those presented by the normal contents of cells; and (4) their great analogy to well-known species of sporozoa recognised as the causes of epithelial proliferation in the intestine, bile-ducts and liver of certain animals—all point forcibly to the conclusion that these bodies, though not necessarily coccidia, are nevertheless protozoa, and are parasitic in cancerous epithelium.* But these opinions by no means pass unchallenged. It is maintained that many of these so-called parasites are nothing more than the appearances produced by the invagination of a part of one cell by the bulk of the substance of another—as might be seen in a section made through the invaginating cell, parallel to, and just below, the surface through which the embedded cell enters (Fig. 70*c*). It is affirmed by others that enclosed leucocytes and degenerative changes have in like manner been misinterpreted. A still more strongly supported suggestion is that these bodies are really due to endogenous formations in the original cancer-cells. This may either occur from an arrest of the process of direct division (amitotic), or from some irregularity in that of indirect division (mitotic, karyokinetic). Round a detached portion of chromatin a cell forms, and grows rapidly, but remains a daughter-cell within the substance of its parent. If this be so, it is difficult to see why daughter and parent should present any marked differences from one another in their staining reactions.

These various objections may doubtless explain many of the appearances described by over-zealous advocates of the parasitic theory; but there remains a considerable residuum not so easily disposed of. In the meantime much of the argument depends on the experience and authority of the different observers; and until the existence of characteristic spores has been definitely made out, or until there is forthcoming such confirmatory evidence as chemistry, and inoculation and cultivation experiments can alone supply (p. 128), the interpretation of the appearances described seems likely to remain more or less in dispute.

* Galloway, Morton Lecture, *Brit. Med. Journ.*, vol. i. 1893.

SECONDARY CHANGES.—The most important is **fatty degeneration.** This occurs in all the varieties of carcinoma. The more rapid the growth, the earlier does this retrogressive change take place, and the greater is its extent; hence it is usually most marked in the *encephaloid* form. It produces softening of the growth, which is often reduced to a pulpy cream-like consistence. **Hæmorrhage, pigmentation, mucoid** and **colloid degeneration** may also occur, with cyst-formation. Cysts may be due also to blocking of ducts—*e.g.*, in the mammæ. **Calcification** and true **ossification** are very rarely met with. Formation of an **abscess** is rare, but important.

VARIETIES.—The varieties of carcinoma are arranged on an anatomical basis. The cells vary markedly in character according as they spring from stratified epithelium, columnar epithelium, or the epithelium of acinous glands. They inherit, to a greater or less extent, the form and tendencies of the variety of epithelium from which they originate. Thus, cells of cancers springing from stratified epithelium tend also to undergo the same epithelial evolution, ending in cornification; and in many cases they show prickle-cells. Columnar epithelium often retains its typical form, and continues to surround open spaces; but in other cases the cells multiply so as to fill the spaces, the outermost cells generally retaining a cylindrical shape. Cells of acinous glands undergo no evolution; by multiplication they produce cells of their own kind, which may be much altered in shape by mutual pressure. Upon this retention by the cells of ancestral, anatomical characters, the chief varieties of cancer are based. Thus we have the **squamous epithelioma,** the **columnar epithelioma,** and the **acinous cancer.** But ancestral peculiarities are not always retained. Certain cancers springing from stratified epithelium—perhaps from the small glands in relation with it—undergo no evolution, and are indistinguishable from scirrhus; while tumours springing from columnar epithelium are in many parts exactly similar to acinous cancer.

In all varieties of carcinoma, the secondary growths tend to repeat the peculiarities of the primary, especially in epithelioma. In scirrhus, the secondary growths in internal organs, though sometimes resembling the primary tumour, are often more rapidly developed. Further, they are softer and more vascular, so that in accordance with the artificial distinction between scirrhus and encephaloid (p. 183), they must be regarded as belonging to the latter variety of cancer.

The name epithelioma was given to cancers springing from the

epithelia, in opposition, as it was thought, to the cancers of connective-tissue origin. The distinction of the forms is of much less importance now that the epithelial origin of all is coming to be more and more recognised. Still, the histological differences between well-marked cases are sufficient to justify a separate description of the above varieties.

Carcinomata are accordingly divided into two groups:—**acinous cancer**, with *scirrhous* or *chronic cancer*, and *encephaloid* or *acute cancer* as subdivisions; and **epithelial cancer**, including *squamous* and *columnar epithelioma*. Of these, columnar-celled epithelioma is most allied in structure to adenoma. *Colloid* or *gelatiniform cancer*, due to colloid degeneration of the cancer-cells, was formerly regarded as a subdivision of acinous cancer, or even as a separate variety; but all the above varieties may undergo this form of degeneration.

CLINICAL CHARACTERS.—Cancers occur with increasing frequency after the age of thirty-five; below that of thirty they are rare tumours. The primary growths are almost always single. They are among the most malignant tumours, there being little ground for choice between them and the sarcomata as regards their mortality. As a group, the cancers grow rapidly, widely infiltrate surrounding parts, early infect lymphatic glands (p. 176), and ultimately become disseminated generally throughout the system. Unless excised very early and very freely, they recur *in loco*. They frequently break down and give rise to very offensive sores which bleed readily.

It will be remembered that while the sarcomata as a group do not infect lymphatic glands (p. 154), they are supposed to generalise more early and more readily than the carcinomata. The reason for this is that the sarcoma-cells frequently form the very walls of the blood-vessels, whilst the cells of cancers do not even come into contact with the walls of the vessels.

Just as the sarcomata vary in malignancy, so also do the carcinomata. On the whole, encephaloid is more speedily fatal than scirrhus, owing to its more rapid growth, greater vascularity and more active epithelial elements. Colloid degeneration seems to diminish malignancy. Every now and again an encapsuled tumour is met with, especially in the soft palate, showing no sign of malignancy, yet having the structure of acinous cancer. In the variety known as atrophic scirrhus, the duration of the disease is not uncommonly from ten to twenty years, and the extension only local and glandular.

Epithelioma is, pathologically, much the least malignant of the cancers. It extends locally, breaks down early, and often infects the neighbouring lymphatics; but it comparatively rarely reproduces itself in internal organs. This is probably owing to the size and character of its epithelial elements, which render them much less liable to transmission by the blood and lymph-streams than the cells of the other varieties of cancer. Its malignancy varies curiously with its seat: thus, on the skin of the face epithelioma has generally a very chronic course, and rarely affects even the glands; on the lip early excision gives a fair chance of cure; on the tongue, its course is often so rapid, affection of the glands so early, and cachexia and death so speedy, that it must be ranked as one of the most malignant tumours.

ACINOUS CANCER.

1. **CHRONIC CANCER** or **SCIRRHUS** is characterised by the amount and density of its stroma and by the slowness of its growth as compared with that of encephaloid. The latter point probably accounts in great measure for the peculiarities in its structure and physical characters.

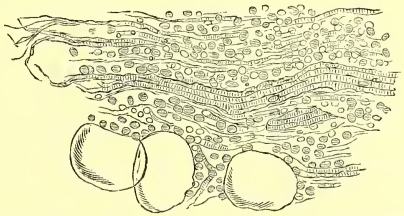


FIG. 73.—*Scirrhus of the Mamma.* A section through the edge of the tumour, showing the small-celled infiltration of the muscular fibres and adipose-tissue in the neighbourhood of the gland. × 200.

The epithelial growth, although at first it may be luxuriant, quickly subsides. The elements soon atrophy and undergo fatty metamorphosis. They are most abundant in the external portions of the tumour where growth is taking place; in the central portions they may be almost entirely wanting. Figs. 73 and 74 show the appearances presented by scirrhus of the mamma in the earlier stages of its development.

The **degeneration** of the epithelial elements is probably due to obliteration of the vessels by the scar-like contraction of the stroma,

which quickly becomes hard and indurated. In this way growth of that part of the cancer is arrested. The whole of the central portions may thus ultimately consist of dense fibroid tissue, amongst which are

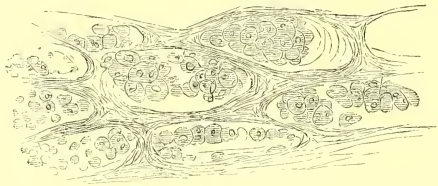
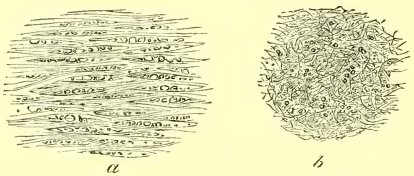


FIG. 74.—*Scirrhus of the Mamma.* A portion of the tumour somewhat internal to that represented in Fig. 73, showing the characteristic alveolar structure of the cancer. × 200.

scattered groups of atrophied epithelial cells and fatty débris (Fig. 75); but even in these cases the epithelial structure is distinctly visible at the periphery. The amount of atrophy and contraction varies considerably in different cases.

The **physical characters** of scirrhus are in the same way due to the abundance of its stroma. The growth is firm and hard, and is usually depressed in the centre, owing to contraction of the fibroid tissue and atrophy of the cells. This is very characteristic of scirrhus



a *b*

FIG. 75.—*Scirrhus of the Mamma.* A section from the more central portions of the tumour, showing the atrophy of the epithelial cells, the diminution in the size of the alveoli, the fibroid tissue, and the fatty débris. *a*. Earlier stage; *b*. more advanced. × 200.

of the breast, where it causes retraction of the nipple and puckering of the skin. The growth is very hard, and creaks as it is cut. The surface of the section is generally "cupped," and of greyish-white, semi-translucent appearance ("like an unripe pear"). It is more or less mottled with dots and streaks of opaque yellow, due to fatty epithelium in alveoli or milk-ducts. The latter may be cystic. The central parts are pale and fibroid; the more external are pinker, because contraction has not obliterated the vessels, and less firm than

the central portions of the growth. They yield, on scraping, a juice which is rich in nucleated cells, free nuclei, and granules. The outlying parts of the tumour can be brought into view by the local application of a five per cent. solution of nitric acid. Opaque white lines mark the affected areas.

By far the commonest seat of scirrhus is the female breast. It is also found in the male breast, the stomach, the liver, the pancreas, the prostate, the skin, and the mucous membranes, where it starts from racemose mucous glands. The secondary growths to which it gives rise are often encephaloid.

2. **ENCEPHALOID** or **ACUTE CANCER** differs from the preceding in the greater rapidity of its growth and in the consequently smaller amount of its stroma, and greater softness of its consistence. Encephaloid and scirrhus cannot be regarded as in any way constituting distinct varieties of carcinoma. There are many intermediate stages between them (scirrho-encephaloid); and all their structural and clinical differences are accounted for by differences in rapidity of growth, which probably depends upon the vascularity of the part in which they are situated.

The epithelial growth in encephaloid is rapid and abundant; the cells, which may be either larger or smaller than those in scirrhus, quickly undergo fatty degeneration, so that often there are more free nuclei visible than cells.

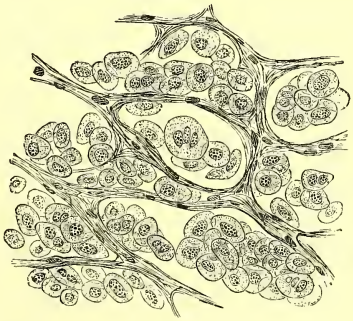


FIG. 76.—*Encephaloid Cancer.* From a secondary cancer of the liver, showing the large size of the alveoli and the thinness of their walls. In the latter, small cells are visible. The large epithelial cells are commencing to undergo fatty metamorphosis. × 200.

The proportion of stroma is very small, and, owing to the rapidity of its growth, it is much less fibrous than that of scirrhus, and does not undergo a similar cicatricial contraction (Fig. 76). The blood-vessels are often very abundant, and the tissue supporting them is soft and non-resistant. Hæmorrhage into these growths is therefore frequent.

Encephaloid cancer is of a soft brain-like consistence, the central portions, where fatty degeneration is most advanced, often being completely diffluent. The tumour is sometimes more or less lobulated.

On section, the undegenerated parts are grey, pinkish, soft and translucent, whilst the degenerated form a white pulpy mass, much resembling brain-substance, which is often irregularly stained with extravasated blood.

Encephaloid is much less common than scirrhous cancer. It is most frequently met with in internal organs as a *secondary* growth. It is sometimes *primary* in the testis and mamma. It may fungate and bleed (fungus hæmatodes). Many growths formerly described as encephaloid cancers were really soft sarcomata (see p. 155).

EPITHELIOMA.

1. **SQUAMOUS EPITHELIOMA** constitutes a tolerably distinct variety of carcinoma, but transitional forms between it and scirrhus are occasionally met with. It always grows from a surface covered by squamous epithelium, either cutaneous or mucous (the junction of the two being a common seat). Its epithelial elements closely resemble those of squamous epithelium.



FIG. 77.—*Cells from an Epithelioma of the Lip.* × 250.

The **cells** (Fig. 77) are often considerably flattened and distorted in shape, owing to the pressure to which, in their growth, they are subjected. The cells grow down from the surface-epithelium into the lymph-spaces of the connective-tissue, and, pushing their way along these, are formed into solid cylinders, which twist about, branch, and intercommunicate—swelling out at some points, and becoming constricted or even interrupted at others Single epithelial cells may be recognised here and there, evidently swept on by lymph. The rods cut across appear as round or oval masses of cells, of which the outermost are usually large, whilst the central are more or less squamous and form a yellowish onion-like mass. Sometimes the central cells appear large and vesicular, whilst the outermost are scaly and flattened. These concentric masses of cells are called "*concentric globes,*" or "*epithelial nests,*" and, though not distinctive or essential, they are exceedingly characteristic of epithelioma. The cells forming them are usually fatty, and may be so closely packed as ultimately to become hard and dry like those of the nails and hair : the globes are

then of a brownish-yellow colour, and of a firm consistence. These globes are often large enough to be readily visible to the naked eye, and, owing to the onion-like arrangement of the epidermic scales, they usually present a fibrous appearance.

The **stroma** presents every variation between rapidly growing embryonic and an incompletely fibrillated tissue. It may be tolerably abundant, or almost entirely wanting. It rarely forms such a marked

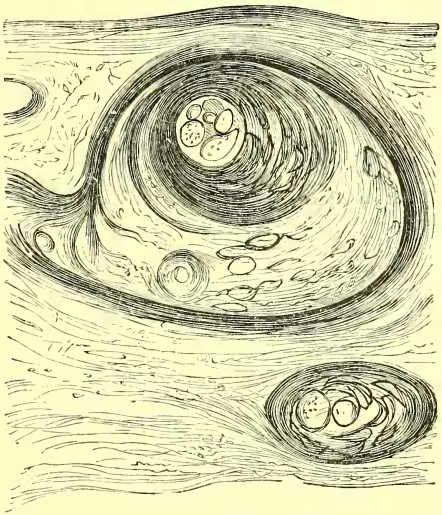


FIG. 78.—*Epithelioma of the Lip.* Showing the concentric globes of epithelial cells. × 100.

alveolar structure as that which characterises the other varieties of carcinoma, and consists simply of the fibrous tissue of the part more or less infiltrated with small round cells, which may be ultimately replaced by connective-tissue (Fig. 79).

The development of epithelioma is due to the down-growth of the surface-epithelium of skin or of certain mucous membranes into the connective-tissue and deeper parts, as is described on p. 166 (Fig. 79). The tendency of epithelioma is to break down at an early stage : this is due to fatty degeneration of the cells and not to inflammation.

Epithelioma usually presents itself as a small hard ulcer, or as an indurated fissure, or as a subcutaneous nodule, which subsequently breaks down. The surface of the ulcer is irregular, and may be sloughy. It is often clean, and covered by large, firm, bluish-red

granulations, consisting largely of epithelium ; more rarely the surface is markedly warty. The tumour itself is firm in consistence, often more or less friable, and on section presents a greyish-white granular

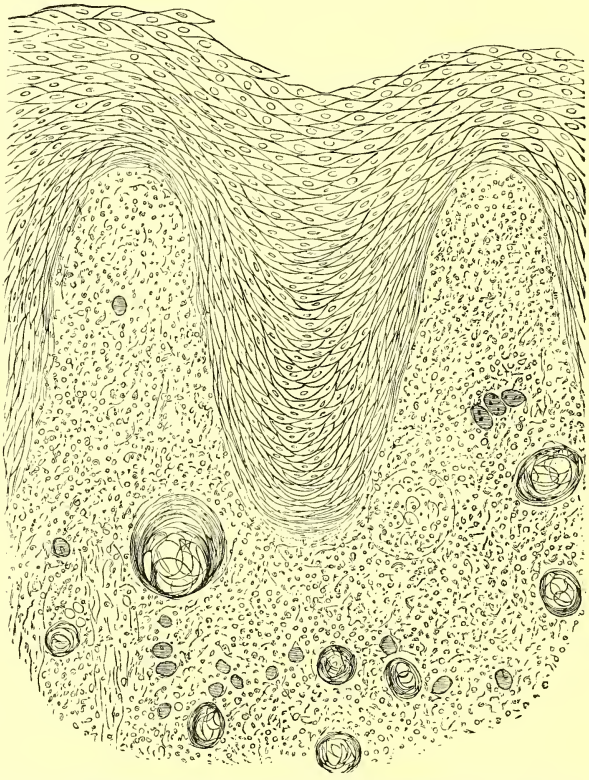


FIG. 79.—*Epithelioma of the Tongue.* A vertical section, showing excessive epithelial growth upon the surface of the papillæ, and extension of the cells into the subjacent connective-tissue. The sub-epithelial tissue is infiltrated with small cells, among which are single epithelial cells and "concentric globes." × 100.

surface, sometimes intersected with lines of fibrous tissue. The cut surface yields on pressure a small quantity of turbid liquid. In many cases a peculiar, thick, crumbling, curdy material can also be expressed, which often comes out in a worm-like shape, suggestive of sebaceous matter from the glands of the skin. This material is very characteristic. It is composed of fatty epithelial scales, and on being

mixed with water it does not diffuse like the juice of other cancers, but separates into minute visible particles. If it is very abundant, the cancer is soft and friable, and the material can be seen on the cut surface as small scattered opaque dots.

Irritation has more to do with the causation of epithelioma than of other kinds of cancer. Some, such as cancer of the scrotum from soot, and epithelioma of the arm in workers with tar or paraffin, appear to be due simply to irritation in people the physiological resistance of whose connective-tissue is diminished until invasion by epithelium is rendered easy. Other epitheliomata occur at points where, the process of development being complicated, errors are likely to have occurred. These places have been already enumerated (p. 125). Many of these are points exposed to irritation. Squamous epithelioma usually infects the lymphatic glands, but rarely occurs in internal organs.

Rodent Ulcer.

Rodent Ulcer deserves a short notice. It is a form of epithelioma beginning as a pimple upon the nose or cheek, and liable to



FIG. 80.—*Rodent Ulcer of Nose.* The patient had small rodent ulcers of the nose and cheek, and an early epithelioma of the lip. × 50. (Boyd.)

frequent irritation from rubbing or picking. After a time it breaks down, and the ulcer thus formed slowly spreads, destroying everything that it meets, including bones, and producing the most hideous deformity. This may go on for many years, the health remaining good and no gland being affected. It differs from ordinary squamous epithelioma chiefly in the small size of the cells, in the absence of prickle-cells, in the slight tendency the cells show to become scaly

and to form nests, and in the ease with which the epithelial columns can be traced (Fig. 80). Some believe that rodent ulcer begins in the root-sheaths of the hairs or in the gland-epithelium of the skin. In some cases having the characteristic history of rodent ulcer, the structure is that of typical epithelioma.

2. **COLUMNAR-CELLED EPITHELIOMA,** or **ADENOID CANCER.** — These terms are applied to those forms of epithelial cancer which grow from mucous membranes with columnar (cylindrical) epithelium—*e.g.*, the stomach and intestines, and especially

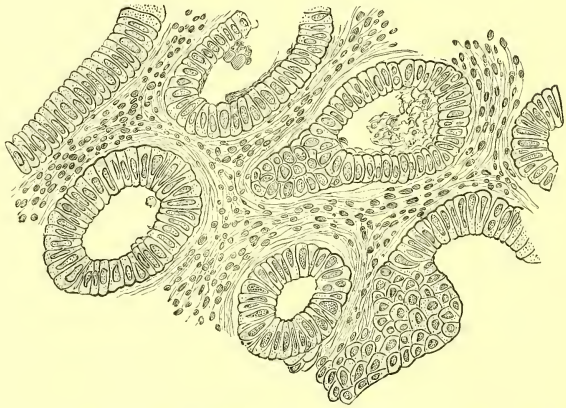


FIG. 81.—*Cylindrical Epithelioma.* From the colon. × 200. Reduced $\frac{1}{2}$.

the rectum and uterus. In these tumours the epithelial elements are similar to those of the mucous membrane from which they grow. They are cylindrical in shape, and are arranged perpendicularly to the walls of the alveoli in a manner precisely analogous to that of the columnar epithelium on the mucous surface (Fig. 81). The slower the growth, the more typical the gland-formation. In rapid growths, and recurrences, the cells are small and the lumina imperfect. The latter may be filled up, and the growth be indistinguishable from acinous cancer, except by its edge, where a low columnar or cubical form usually persists; but this too may be lost. The growths are of a soft, and often gelatinous consistence; they show a marked tendency to undergo colloid degeneration. These tumours cause secondary growths in the lymphatic glands, and sometimes in the liver, lungs, and bones: the secondary tumours possess the same characters as the

primary cancer. The distinction between adenoid cancers and simple adenomata depends upon the invasion of the neighbouring tissues by the former.

Colloid Cancer.

Colloid, or **Gelatiniform** cancer, is simply one of the preceding forms which has undergone a mucoid or colloid change. Sarcomatous and other non-cancerous growths may undergo the same change.

The alveolar structure in colloid cancers is very marked. The

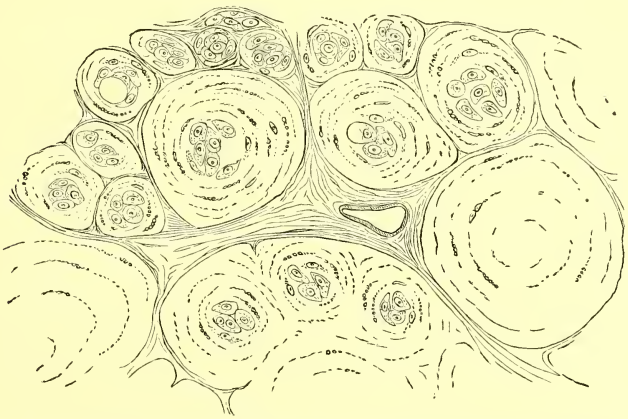


FIG. 82.—*Colloid Cancer.* Showing the large alveoli, within which is contained the gelatinous colloid material. × 300. (Rindfleisch.)

alveoli have very thin walls; they are large, distinct, and more or less spherical in shape. The large size and distinctness of the alveoli is owing to their distension by products of degeneration. These products form a gelatinous colloid material, which is glistening, translucent, colourless, or yellowish, and of the consistence of thin mucilage or size. In the main it is perfectly structureless; within it, however, are embedded a varying number of epithelial cells (Fig. 82). These cells present a peculiar appearance: they are large and spherical in shape, and are distended with drops of the same gelatinous material as that in which they are embedded (Fig. 82). Many of them display a lamellar surface, their boundary being marked by concentric lines. It would appear that the colloid change commences in the cells, which become gradually destroyed in the process.

In other cases, similar to the naked eye, the cells with the exception of slight fatty metamorphosis, are but little affected, and the substance distending the alveoli is more viscid and mucoid in character. This is due to a **mucoid degeneration** (p. 66) of the intercellular substance rather than to a colloid change commencing in the cells.

Colloid cancer is most frequently met with in the stomach, intestine, ovary, and peritoneum. In the latter case it is either secondary or the growth is a sarcoma. The tendency of abdominal tumours to undergo colloid degeneration is at present unexplained.

CHAPTER XVI.

THE TERATOMATA.—CYSTS.

The Teratomata.

These tumours are congenital. They occur chiefly in the sacral region (coccygeal tumours), and about the head and neck—points at which double monsters are united; but they may be internal. Some of them are due to the inclusion and imperfect development of one fœtus within another; others to the abnormal development of the tissues of a single fœtus. They are most complex and may contain all the tissues of the body up to ganglion cells, more or less confusedly mixed. They may be very large at birth, or may not attract notice till later. Dermoid cysts belong to this group.

Cysts.

In addition to the new growths already described, there is a large class of formations, many of which cannot be regarded as "tumours," in the strict application of this term. These are the **cysts** or "**cystic tumours.**"

A **cyst** is a cavity containing liquid or pultaceous material, which is separated from the surrounding structures by a more or less distinct capsule. It may be (1) a new formation; or (2) a pre-existing structure which has become distended either by its own secretion, or by the extravasation of some other fluid into it. Only the former comes within the category of new growths; but, for the sake of conveni-

ence, it will be advisable to consider them both in the present chapter.

There are thus two principal modes by which cysts originate. The first, and most frequent, is by the gradual accumulation of substances within the cavities of pre-existing structures. These substances are, for the most part, products of the parts in which they are found—being in some cases a secretion, and in others a cell-growth. The second, and less frequent, mode of origin is by the independent formation of a cyst in the tissues.

The accumulation of secretions and of other products within pre-existing cavities may be effected in the three following ways :—

1st. By the retention of the normal secretion owing to the closure of the excretory ducts—as so often occurs in sebaceous glands.

2nd. By excessive secretion, the cavity being unprovided with an excretory duct—as in the distension of bursæ.

3rd. By the extravasation of blood into the cavity—as in hæmatocele.

The independent formation of a cyst may take place :—

1st. By the softening and liquefaction of the tissues in some particular part, owing to mucoid or fatty changes. The tissues around the softened matters become condensed, and ultimately form a kind of cyst-wall.

2nd. By the collection of fluid in certain connective-tissue spaces, and the subsequent enlargement and fusion of these spaces. The surrounding tissue becomes condensed, and forms a cyst-wall; and this may in some cases become lined with flattened connective-tissue cells (endothelium).

3rd. By the formation of a cyst-wall round foreign bodies, parasites, or extravasated blood: the wall consists of fibrous tissue, and is the result of a chronic inflammation. Smooth, heavy, sharp-edged foreign bodies are particularly liable, during the process of "healing in," to produce cysts of this character, especially when the parts are not kept at rest. Salzer has suggested the artificial introduction of such substances when adhesions are feared or a false joint desired.

Structure.—The **wall** of the cyst will vary in its nature according as it is that of a pre-existing or a newly formed cavity. In the former case, it will possess an epithelial lining which will present the same characters as that of the gland, serous membrane, or other structure from which the cyst originated. If the cyst is of independent forma-

tion, there is at first no endothelial lining to the fibrous capsule, but one may develop later, as in false bursæ. The cyst-wall is sometimes firmly connected with the adjacent parts, so that it can only with difficulty be separated; in other cases the union is much less intimate. Instead of being a distinct structure, it may simply consist of the surrounding tissue which has become dense and fibrous in character.

The **contents** of cysts are very varied, and may serve as a basis for their classification. In the retention-cysts, they will vary with the nature of the normal secretion. Serum, sebaceous matter, saliva, milk, seminal fluid, and other substances are found in these cysts: they are more or less altered in character from having been retained in a closed cavity. In the exudation-cysts, serum is the most frequent constituent; and in extravasation-cysts, blood. In those cysts which originate from the softening and breaking down of tissue, the contents are formed from the products of retrogressive tissue-metamorphosis, such as mucin, fatty matters, and serum.

Cysts may be **simple** or **compound**. A simple cyst consists of a single loculus. A compound or multilocular cyst is one consisting of numerous loculi, which either communicate with one another or remain isolated. Another variety of compound cyst is one with endogenous growths, or, in other words, a large cyst with others growing in its walls. A compound cyst may become a simple one by the destruction of its walls.

Cysts are frequently associated with other growths, hence the terms —"cystic sarcoma," "cystic cancer," &c. It is especially in those growths which originate in glandular structures, as in the mamma, testicle, and ovary, that this combination is met with. The cystic development may almost entirely obliterate the structure of the tumour in which it takes place, so that ultimately the latter may become converted into a mere congeries of cysts. In other cases large papillary masses of the tumour grow into the cystic cavities ("compound proliferous cysts"). Considerable difficulty in determining the nature of the original growth is thus not infrequently experienced.

Secondary Changes.—These may take place in the wall of the cyst or in its contents. The cyst-wall itself may become the seat of new growths, and produce secondary cysts, villous, glandular, and other structures: this process occurs in many compound ovarian cysts. It may also be the seat of an inflammatory process, which terminates in suppuration and granulation: by this means the cyst frequently

becomes obliterated, its contents being either absorbed or discharged externally, and the cavity closing by granulation. Calcification and ossification of the wall may also occur. The contents of cysts undergo various changes, owing to their retention in a closed cavity. The secretions become altered in character, thickened, and viscid. Epithelial elements undergo fatty changes, and so give rise to cholesterin crystals. Calcification of the contents is also common.

CLASSIFICATION.—Cysts may be most conveniently classified according to their mode of origin, thus :—

I. *Cysts formed by the accumulation of substances within the cavities of pre-existing structures.*

A. **Retention Cysts.**—Cysts resulting from the retention of normal secretions. These include—

a. Sebaceous Cysts.—These are formed by the retention of secretions in the sebaceous glands. They possess a very thin connective-tissue wall lined by stratified epithelium (Fig. 83). They contain a mass of fatty epithelium and its products, cholesterin and amorphous débris.

β. Mucous Cysts.—These are formed by the retention of secretions in the glands of mucous membranes.

γ. Cysts from the retention of secretions in other parts, including—*ranula,* from occlusion of the salivary ducts; *encysted hydrocele,* from occlusion of the tubuli testis; *mammary cysts,* from obstruction of the lacteal ducts; *simple and some compound cysts of the ovary,* from dilatation of the Graafian follicles; and simple *cysts of the liver and kidneys* from local obstruction.

B. **Exudation Cysts.**—Cysts resulting from excessive secretion in cavities unprovided with an excretory duct. These include *bursæ, ganglia, hydroceles, meningoceles, cystic bronchoceles,* and many *cysts in the broad ligament.*

C. **Extravasation Cysts.**—Cysts resulting from extravasation into closed cavities. These include *hæmatocele,* and some other forms of sanguineous cysts.

II *Cysts of independent origin.*

A. **Cysts from Softening of Tissues.**—These are especially common in new formations, as in chondroma, lipoma, sarcoma, &c.

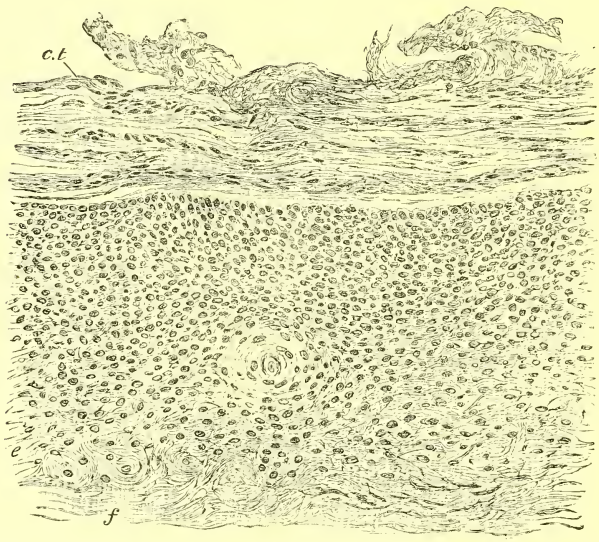


FIG. 83.—*Sebaceous Cyst. c.t.* The thin connective tissue layer forming the wall, lined by a thick layer of epithelium. The outer cells of this are somewhat cubical, then, passing inwards, they become flattened, and finally they enlarge considerably, become fatty and rather suddenly cease to stain. They are succeeded by fatty débris (*f*), so compressed as to have a fibrous aspect. (Boyd.)

B. **Cysts from Extravasation into Solid Tissues**—*e.g.*, into brain, or soft new-growths.

C. **Cysts from Expansion and Fusion of Spaces in Connective Tissue.**—These include—

a. *Bursæ,* originating from irritation and exudation into the tissues.

β. *Serous cysts in the neck,* "hygromata" (p. 195).

γ. *Many compound ovarian cysts.*

D. **Cysts formed around Foreign Bodies, Extravasated Blood, and Parasites.**

E. **Congenital Cysts.**—Many *hygromata* (persistent fœtal structures). *Dermoid cysts.* Sometimes these appear to be the remains of blighted ova, but usually they are due to inclusion of a piece of epiblast. Their wall has more or less perfectly



FIG. 84.—*Dermoid Cyst of the Ovary.* Showing all the structures of true skin except sweat-glands—viz., Epithelium, rudimentary papillæ, fibrous tissue or cutis vera, hair follicles, large sebaceous glands. × 18. (Boyd.)

the structure of skin (Fig. 84); they may contain fatty matters, coils of long hair, teeth and bones. Even rudimentary mammæ have been found in them.

CHAPTER XVII.

DISEASES OF THE BLOOD.

ANÆMIA.

THE term anæmia has no very definite connotation. As generally employed, it includes all diseases of the blood which are characterised by a deficiency in the number of the corpuscles or a diminution in the total percentage of hæmoglobin. Other expressions with a more

precise significance are sometimes used. Thus a diminution in the number of red corpuscles is known as *oligocythæmia* or *aglobulism*, and a deficiency in the hæmoglobin, as *achromatosis*. These results may be produced by temporary conditions. Thus, anæmia is common during convalescence from acute fevers, and after severe hæmorrhages. It may also owe its origin to deficiencies in the ingesta, or to that which produces the same practical result—stricture of the œsophagus or of the pylorus. In cases due to these causes the number of red corpuscles is always reduced; while the leucocytes may be either slightly diminished or slightly increased. Not only is the total percentage of hæmoglobin below the average, but the amount contained in each corpuscle is less than normal. Anæmia following acute fevers or hæmorrhage rapidly disappears: the exact rate of disappearance varying with the nature and severity of the disease, the recuperative power of the patient, and the general conditions of convalescence.

To two varieties of anæmia special reference must be made. These are (1) Chlorosis, and (2) Pernicious Anæmia.

I. Chlorosis.

Chlorosis is mainly a disease of girls and young women. It takes its name from the effects of its most marked feature, which is the **deficiency of hæmoglobin**. This is so great that the **skin** and **mucous membranes** of the patient assume a very pale and slightly green tinge. In extreme cases the hæmoglobin may fall to one-eighth of its full amount, and in most it is less than a third. The **fall in red corpuscles** is by no means parallel. In mild cases they may average 3,500,000 to the cubic millimetre; and they seldom fall below 2,000,000. The corpuscles are on the whole distinctly smaller than usual. Some of them are very small, ranging down to 3μ in diameter (microcytes); a few are large, with a diameter up to 12μ (macrocytes); while others with an irregular outline are occasionally found (poikilocytes). The **specific gravity** of the blood may fall ten to twenty degrees, thus furnishing reliable evidence of its "watery" condition. In some few cases, where death had occurred, the heart and large arteries were unusually small. Other morbid conditions secondary to the changes in the blood may coexist. Among these are dyspnœa and the occasional deposit of fat, both resulting from the deficient oxygen-carrying power of the blood; slight œdema,

probably from defective nutrition of the vessel-walls; and various auscultatory signs due to the lowered specific gravity of the blood and defective action of the inadequately nourished heart.

PATHOLOGY.—No generally accepted explanation of the changes in the blood has yet been found. Virchow first drew attention to the small size of the heart and large arteries, and attributed it to defective development. He regarded the disease as the expression of an inability of the blood-forming organs to meet the demands made upon them during a period of rapid development; a disease especially liable, therefore, to occur in those in whom these parts are congenitally defective. In many cases the generative organs are also backward in their development; and this fact undoubtedly affords some support to Virchow's theory. Still the enormous frequency of the disease, its practical limitation to one sex, its ready curability, and the want of parallel between the great fall in hæmoglobin and the slight fall in corpuscles, point to a more transient and less organic causation. It is unquestionable that gastralgia, gastric catarrh, gastric ulcer, *constipation*, defective hygienic surroundings, and irregular habits are frequently associated with the condition; and that, in many examples of the disease, the administration of iron fails to effect a cure until these be relieved. On the other hand, it is no less certain that the relief of these conditions without the administration of the iron is ineffectual as a cure, in all but the mildest forms. Now it is notorious that hæmoglobin, which contains a very appreciable amount of iron, is the progenitor of pigments which contain little or none. The amount of this metal excreted in the fæces and the urine is excessively small, and is not appreciably increased in anæmia. It seems reasonable to suppose that the iron thus left behind is utilised by the newly-forming hæmoglobin; and if therefore the hæmoglobin in the blood is deficient, it would seem more rational to look for a cause that interferes with the synthesis of hæmoglobin from the accumulating stock of iron, rather than for one which leads to any loss in the total amount of iron contained in the body. Any supply of iron in addition to that already stored in the liver, needed to meet the demands of growth and waste, must clearly come from the food. Much evidence is available to show that most, if not all, the iron absorbed or excreted is absorbed or excreted in *organic* forms only, though it is impossible to deny that it may exist in an inorganic form in the portal vessels, and be retained and recombined in the liver.

According to Bunge, the immediate precursor of hæmoglobin is hæmatogen, a nuclein containing iron, phosphorus and proteid matter. He suggests that the sulphuretted hydrogen, developed in the alimentary tract of dyspeptic and constipated persons, seizes on the organic iron (hæmatogen) in the food and converts it into sulphide, which is incapable of absorption. Thus the body is starved of iron, and chlorosis results. The success following the administration of large doses of iron he explains by supposing that the attraction of the sulphuretted hydrogen for the *inorganic* salts is so great that the organic compounds are undisturbed and allowed to pass on into the body. Sulphuretted hydrogen is very diffusible and is very readily absorbed. Its destructive action on organic iron compounds is therefore not necessarily limited to the intestine, but might easily be exercised in the blood itself. Stockman has published some cases in which sulphide of iron enclosed in capsules to protect it from the action of the gastric juice was followed by distinct benefit. The sulphide could not have attracted any of the sulphuretted hydrogen away from the organic iron. The failure of both bismuth and manganese to act in the same way as curative agents also casts additional doubt on the sufficiency of Bunge's theory, as also does the success which has attended the subcutaneous injection of very small doses of iron.

Among other theories may be mentioned Landwehr's. This observer is of opinion that, at the age anæmia is common, there is a tendency to the excessive formation of animal gum (the carbo-hydrate constituent of mucin), which is needed for the embryo. This, when present in excess, may interfere with the formation of hæmoglobin.

Zander attaches much importance to a supposed deficiency in the hydrochloric acid contained in gastric juice. But this deficiency is not uniform. The gastric juice of some cases of chlorosis contains a large excess of hydrochloric acid, which is perhaps partly responsible for the occasional development of acute gastric ulcers. Further, the administration of this acid has no curative value in anæmia. The disease is therefore unlikely to be due to a want of it.

II. **Pernicious Anæmia.**

Pernicious anæmia differs from chlorosis in many particulars. It does not show the same preferences as regards age and sex, being commoner in older persons and in males. It is, moreover, generally fatal.

Pernicious anæmia may be the apparent result of hæmorrhage after childbirth, or of any of the ordinary antecedents of anæmia already mentioned. More often it has no obvious cause.

APPEARANCES. The **blood** in pernicious anæmia is very different from that in chlorosis. It differs from it in three especially important particulars. (1) In chlorosis the most marked feature is a drop in the *percentage* of hæmoglobin, whereas in pernicious anæmia the most marked feature is the **diminution** in the number of **red corpuscles.** Thus, although the total amount of hæmoglobin is invariably diminished, yet the amount contained in each corpuscle may even be in excess of the normal. The fall in the percentage of red corpuscles is enormous. Blood with only 300,000 red corpuscles to the cubic millimetre has been described.

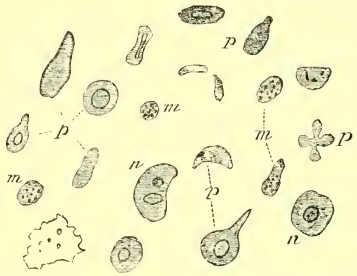


FIG. 85. — *Pernicious Anæmia.* Blood corpuscles showing poikilocytes (*p*), microcytes (*m*), and nucleated corpuscles (megalocytes) (*n*). Preserved in Hayem's fluid.*
(Specimen and drawing by Dr. Mott.)

(2) The next most characteristic difference is the frequency of **changes** in the **form** and **size** of the **corpuscles.** Sometimes there are found, as well as normoblasts, enormous nucleated red corpuscles (20μ dia.) known as giganto-blasts (Fig. 86). According to Eichhorst, the microcytes are not only much more numerous than in chlorosis, but have a very characteristic appearance. They are spherical, granular, and highly pigmented. The number of leucocytes and of blood platelets is somewhat diminished, the tendency to the formation of rouleaux is less marked, and the coagulating power of the blood is feebler. (3) The total **quantity of blood** is most markedly **diminished.** At a post-mortem examination the vessels are almost empty. If this fact be considered in connection with the percentage-fall in red corpuscles, and the diminished specific gravity of the blood (1028), some idea can be formed of the enormous extent of the change, so far as the blood is concerned.

The **marrow** of the long bones is generally red, and contains less fat than normal. Large numbers of giganto-blasts are found, and

* Perchloride of mercury, 0·5 grm.; chloride of sodium, 1·0 grm.; sulphate of sodium, 5·0 grm.; distilled water, 200·0 c.c.

there is also an increase of normoblasts, and often in great numbers of microcytes. The red marrow contains pigment, giving the iron



FIG. 86.—*Pernicious Anæmia.* Fresh marrow from humerus. Appearance of yellow marrow is not unlike that of raspberry jam. Ordinary marrow cells are shown (*o.m.c.*). The shaded cells are pigmented marrow cells forming blood-corpuscles; the larger are megaloblasts and the smaller normoblasts. The cells marked (*f*) show multiplication by fission, those marked (*g*) multiplication by gemmation. Marrow treated with Hayem's fluid and teased.
(Specimen and drawing by Dr. Mott.)

reaction (see below). The finer bony trabeculæ occasionally become absorbed.

The changes in the **liver** are of considerable importance. In the centre of the lobule there may be an excess of pigment, and in the peripheral zone iron, so loosely combined with organic matter that a distinct blue coloration can be obtained on treating sections of the organ with ferrocyanide of potassium and dilute hydrochloric acid. The cells in the immediate neighbourhood of the intralobular veins are occasionally fatty.

The **heart** and smaller blood-vessels, and occasionally the intima of the large arteries, show extensive fatty changes, from which the

skeletal muscles are practically free. The changes in the heart are particularly well marked. In the left ventricle the fatty areas are so distinct that the terms "thrush-breast" and "tabby-cat" have been

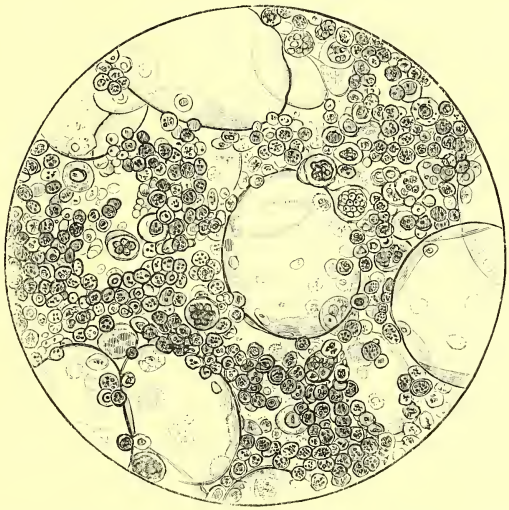


FIG. 87.—*Pernicious Anæmia.* Same marrow as in Fig. 86, but hardened in Müller's fluid and cut in celloidin. Some half-dozen fat vesicles are seen, with the intervening capillaries much dilated. These contain normoblasts with rosetted nuclei. The smallest cells are microcytes: those of intermediate size are granular-looking red corpuscles.

(From a specimen by Dr. Mott.)

used to denote them. The **subcutaneous fat** is very generally increased. The **skin** acquires a faint yellowish or "old wax" colour, suggestive of slight jaundice. Small **hæmorrhages** are common in many parts. Flame-shaped hæmorrhages clustered round the disc are particularly frequent in the **retina**, and are an important aid to diagnosis. Exacerbations are accompanied by fever. The **urine** is generally dark. An excessive amount of urobilin is excreted. This is shown by the absorption-band at F when the urine is examined spectroscopically.

PATHOLOGY.—Besides the differences above mentioned, which may be held to mark off chlorosis from pernicious anæmia, there is the additional evidence which is gained by the administration of iron,

This drug, which effects a cure in chlorosis, is utterly useless in pernicious anæmia.

The increase of iron in the liver and marrow, and of urobilin in the urine, affords evidence that the disease is due to the excessive destruction of red blood-cells—hæmolysis. The changes in the marrow of the long bones and the existence of nucleated corpuscles in the blood is no argument against this view, as they might be due to increased physiological, not to pathological, hæmogenesis. This explanation is the more probable, as repeated bleedings of animals produce similar effects. A somewhat similar condition has been produced in the liver by the administration of toluydene-diamine. This discovery has led to the suggestion that the disease is due to the absorption of toxic products from the intestine. If this be correct the "poison" must be some definite substance or organism which very rarely finds its way into the blood; for while ulceration of the intestine and all manner of decomposition of its contents are common enough, pernicious anæmia itself is comparatively rare. The gradual progress and persistence of the condition is also much against a purely chemical cause, unless it be the product of some organism which takes up its abode in the intestine without producing any local irritation. Two observers have described organisms, but their results have not yet been confirmed.

It is worthy of note that while in phosphorus-poisoning the fatty degeneration is almost universal, in pernicious anæmia it is far more marked in the heart than elsewhere. Mott has suggested that, while the feeling of languor so characteristic of the disease imposes rest upon the skeletal muscles, the deficient quantity and diminished oxygenating capacity of the blood necessitates increased work on the part of the heart. The balance of work and repair in the organ cannot, therefore, be maintained, and degeneration ensues to a much greater extent than elsewhere.

LEUCHÆMIA.

Leuchæmia, or leucocythæmia, is a disease characterised by a considerable and permanent increase in the number of white corpuscles of the blood, by a diminution in the number of the red corpuscles, and by enlargement of some of the lymphatic organs. The lymphatic organ most frequently involved is the spleen. This is enlarged in the great majority of cases (Splenic Leuchæmia). The enlargement of the spleen is sometimes associated with enlargement of the lymphatic

glands, and sometimes, although much less frequently, with changes in the medulla of bones. In very rare cases the lymphatic glands only are involved (Lymphatic Leuchæmia), and cases have been described in which the osseous medulla is principally affected (Myelogenic Leuchæmia). The lymphoid tissue of the intestine may be hypertrophied. In most cases of leuchæmia an overgrowth of lymphatic tissue in other organs occurs in the course of the disease.

Leucocytosis.—Before proceeding to the consideration of leuchæmia, it will be well to allude to that slight and temporary increase in the number of white blood-corpuscles which has been termed "leucocytosis." This differs from leuchæmia in these respects—that the increase in the number of white corpuscles is only *temporary*, is not necessarily associated with any diminution in the number of the red, and is never so marked as in leuchæmia, in which there are always more than one white to every twenty red corpuscles. Moreover, in leucocytosis the increase is almost limited to the *multinucleated* leucocytes. A slight and temporary increase in the number of white blood-corpuscles occurs in many conditions. Physiologically, it occurs after a meal, and in the later months of pregnancy. In pyæmia, and in many of the acute pyrexial diseases, especially those in which there is acute swelling of lymphatic structures, such as typhoid and scarlet fever, there is often a marked excess of white corpuscles. The same change has been described in tubercular diseases and in conditions accompanied by suppuration. After large losses of blood, also, there is an increase, owing to the pouring of lymph into the blood to make up its mass. Leucocytosis does not seem to interfere either with the circulation or with the general health.

PATHOLOGY.—The pathology of leuchæmia is still exceedingly obscure, and will probably remain so until our knowledge of the physiology of the blood and the origin and fate of the blood-corpuscles is more complete. Physiologically, we know that the white corpuscles originate in the lymphatic organs, from which they pass into the blood, either directly or through the lymphatic vessels. Owing to the enlargement of one or more of the lymphatic organs which always exists in leuchæmia, it has been supposed that the increase in the number of the white corpuscles which characterises the disease, is due to their excessive production by the enlarged organs, such as occurs in some cases of leucocytosis. Inasmuch, however, as there is not only an increase in the number of white, but a diminution in the number of

red, this hypothesis is insufficient to account for the change. Further—lymphatic organs may become enormously enlarged without the production of any leuchæmia. This occurs, for example, in the spleen in **Splenic Anæmia,** which disease, but for the fact that there is no increase in white blood-corpuscles, is similar to leuchæmia. It also occurs in the lymphatic glands in Hodgkin's disease. The other view, promulgated by Virchow, is that the transformation of white corpuscles into red is diminished. Hence the former tend to accumulate and the latter to disappear. Against this view it may be urged that there is no constant proportion between the increase of the white and the diminution of the red; and that many of the leucocytes show evidence of active growth, not of diminished vitality. It must also be remembered that the origin of red corpuscles from leucocytes is by no means certain; while it is quite certain that they are the offspring of the nucleated red corpuscles found in the red marrow of bone. It is quite possible that the different varieties of leuchæmia have each a different pathology.

APPEARANCES.—Blood.—The increase in the number of white corpuscles varies very considerably in different cases. A proportion of one white to ten red is quite common, and often there are as



FIG. 88.—*Leuchæmic Blood.* From a young man with enormous enlargement of the spleen. × 200.

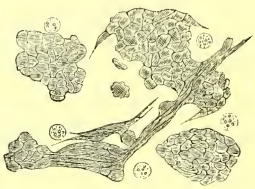


FIG. 89.—*Blood from a case of Splenic Anæmia.* From a middle-aged man with great enlargement of the spleen. × 200.

many as one to three (Fig. 88). This increase gives to the blood a paler and more opaque appearance than is natural. In the earlier stages of the disease the proportion may not be more than one to twenty.

In *splenic leucocythæmia* it is the large mononucleated corpuscles which are particularly abundant, and in *lymphatic leucocythæmia* the smaller lymphocytes. In the *myelogenic form* the nature of the new cells is less certain. Among the new elements found in the blood in this variety are: (1) large mononucleated neutrophile cells closely

resembling "marrow cells;" (2) nucleated red corpuscles suggestive of normoblasts; and (3) eosinophile cells, and cells with "mast-cell" granules.

It has often been affirmed that the new corpuscles, when examined on the warm stage, show no amœboid movements. This observation, together with the fact that fatty degeneration has been occasionally observed, has led to the belief that the majority of the leucocytes are dead. Muir has lately pointed out that the absence of movement is confined to the large mononucleated variety, and that any multinucleated leucocytes present exhibit their normal motility.

The red corpuscles, like the white, vary in their numbers. They may be reduced to one half or a quarter the normal. They are usually natural in appearance, but sometimes they are distinctly paler than in health. Occasionally they appear to be unusually soft, and exhibit a tendency to stick together instead of forming the natural rouleaux. In the case of *splenic anæmia*, referred to on p. 207, these characters were especially marked (Fig. 89). The diminution in the number and the impairment of the quality of the red corpuscles, which exist not only in leuchæmia, but in most cases of great splenic enlargement, account for the anæmia which exists in these conditions. In addition to the red and white corpuscles, nucleated red corpuscles have been found in leuchæmic blood; and minute, colourless, long, slender octohedral crystals of an albuminous character have been discovered in the blood, liver, and spleen. The coagulating power of the blood in leuchæmia is much diminished, and when this liquid is allowed to stand the white corpuscles form a creamy layer upon its surface.

Spleen.—In this, which is much the most important organ in the production of leuchæmia, the change is characterised mainly by increased growth. The organ becomes enlarged, often enormously so. The enlargement is uniform, so that the shape of the organ is but little altered. The capsule is often thickened, and there are usually adhesions with the adjacent viscera. The consistence of the spleen in the later stages is firmer than natural. The cut surface is smooth, and of a greyish or brownish-red colour, while thickened trabeculæ can often be seen marking it as whitish lines. The Malpighian corpuscles, although they may be slightly enlarged in the earlier stages of the disease, are seldom prominent, and they are often invisible when the splenic enlargement is advanced. In exceptional cases, however, and especially when the lymphatic glands are involved, they may form prominent growths. Sometimes wedge-

shaped masses, of a dark-red or reddish-yellow colour, are seen near the surface of the organ. These are probably infarctions of embolic origin.

When the spleen is examined microscopically, its structure is found to be but little altered, the enlargement being due mainly to an increase of the splenic pulp. The trabecular tissue is also increased and thickened, and this change advances with the continued enlargement of the spleen. The Malpighian corpuscles are but little increased in size: sometimes they are atrophied.

Lymphatic glands.—The enlargement of the lymphatic glands is much less in splenic leuchæmia than in those cases in which the glands are primarily and principally affected. In splenic leuchæmia one or more groups of glands are slightly enlarged in about one-third of the cases. The glands are rarely increased in consistence, and are usually freely movable. On section they are of a greyish-red colour, and are often mottled with hæmorrhages. Microscopically, the enlarged glands show increase of the pulp and blocking of the lymph channels.

The **red marrow**, found normally in the bones of the head and trunk of adults and throughout the limbs in the fœtus, is a blood-forming organ. In leuchæmia it may become more highly cellular, and consequently softer, and greyer or yellower in colour. Further, whereas in normal growth the red marrow is replaced by yellow progressively from the toes and fingers up to the heads of the femora and humeri, in this disease the opposite change occurs, and the yellow marrow is progressively transformed into red from the trunk towards the extremities of the limbs.

The **follicles of the intestine** may become so much enlarged as to form distinct projections from the mucous membrane, although this is less common than in Hodgkin's disease.

Other organs.—In the course of the disease, masses of lymphatic tissue or of lymphoid cells usually appear in places otherwise free from them. These masses are principally found in the liver and kidneys, less frequently in the lungs and muscles. The new growth in these organs sometimes forms distinct tumours, but much more commonly exists as an infiltration. How far these lymphoid growths are the products of a hyperplasia of the cells in the interstitial tissue of the organ in which they are situated, and how far they are the result of emigration of the leucocytes, which exist in such large numbers in the blood, is unknown. The former, however, is probably the most important factor in the process.

The organ which is most frequently affected is the **liver**. Here, in leuchæmia, the vessels generally are enlarged and distended with white blood-corpuscles. Accumulations of corpuscles and lymphoid tissue are seen between the acini, and extending along the intercellular network into the acini themselves, so that the lobules are sometimes seen to be clearly mapped out by a greyish-white interlobular infiltration. As this increases, the liver-cells become compressed and atrophy, until ultimately the lobules may be entirely replaced by it. This is

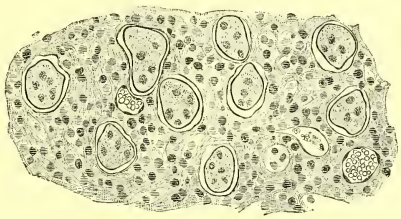


FIG. 90.—*Liver from a case of Splenic Anæmia.* Showing the extensive cellular infiltration involving the intercellular network. The organ was greatly enlarged, and the new tissue was visible to the naked eye between the acini. × 200.

well-shown in the liver from the case of splenic anæmia (Fig. 90), the blood from which is represented in Fig. 89. Associated with this infiltration there is often a formation of small, round, whitish lymphoid nodules, somewhat resembling grey tubercles. These also are situated in the interlobular tissue. Owing to these changes, the liver becomes very considerably increased in size.

In the **kidneys**, which are also frequently affected, the change is similar to that in the liver. Here also it consists for the most part in an infiltration, with which may be associated the formation of roundish nodules and masses.

CHAPTER XVIII.

DISEASES OF THE CIRCULATION.

THE efficiency of the circulation depends on the maintenance of a correct relationship between the action of the heart, the size and elasticity of the blood-vessels, and the quantity and composition of the blood, as well as on the maintenance of a healthy lining membrane

throughout the whole of the vascular tract. It is altogether out of the scope of this work to deal fully with the many ways in which these various factors may deviate from the standard of health. Practically, in disease, they are nearly always combined. Structural diseases of the heart, arteries, and veins, together with their results on the general circulation, will be dealt with subsequently. We shall here limit ourselves to a brief review of the causes and effects of both **diminution** and **increase in the blood supply** of a part, and then deal at greater length with the phenomena of **mechanical congestion, dropsy, thrombosis,** and **embolism.**

LOCAL ANÆMIA.

By **local anæmia** is meant diminution in the amount of blood in a part owing to deficiency of the supply. It may be partial or complete.

CAUSES.—The causes of diminished arterial supply comprise all those conditions which either narrow or completely close the lumen of the supplying artery. The lumen of an artery may be diminished by disease of its walls—atheroma, calcification, or syphilitic thickening; or by pressure exercised upon it from without, as by new growths, constricting scars, inflammatory exudations and mechanical effusions, especially in unyielding tissues, as bones or tendon-sheaths. Complete closure of the vessel may result from some of the foregoing conditions, or, more commonly, from thrombosis, embolism, or ligature. In some cases the supply of blood is diminished by an increase in the natural resistance, from irritation of the vaso-motor nerve. This occurs in some neuralgic and other nervous affections, or from the action of certain substances, such as ergot of rye and opium, or, again, merely as the result of a low temperature. It is sometimes attributed to the presence in the vessels of products of metabolism, either in excessive amount or of abnormal character. Anæmia of one part may be secondary to hyperæmia of other parts, such as anæmia of the brain and skin in congestion of the abdominal viscera; or it may be due to a general diminution of the total quantity of blood, as after hæmorrhage, in which case the distal parts suffer most.

RESULTS.—A part with a diminished arterial supply is usually paler, less tense, and of a lower temperature than natural. Its

nutrition and function also are impaired, so that it may undergo fatty degeneration, atrophy, or death. These results have been exemplified in the chapters on Fatty Degeneration, Atrophy, and Necrosis.

Obstruction of a large artery causes rise of pressure (transient under healthy conditions) everywhere except in its own area; and this increased pressure endangers the safety of delicate or diseased vessels, until the extra blood thrown into the suddenly curtailed vascular system is accommodated in some way. The heightened pressure affects the vaso-motor centre, and this speedily produces dilatation of vessels sufficient to restore the normal pressure. But the vessels which dilate most markedly and persistently are those going to the anæmic part and anastomosing with branches from the trunk beyond the obstruction; this is probably owing to some obscure vaso-motor mechanism, excited, it may be, by the anæmia. These "collateral" vessels become larger, longer (tortuous), and thicker, until the circulation in the part has again become normal—*i.e.*, **collateral** circulation is established. At first, all vessels having anastomoses with the obstructed one probably dilate; but those which enlarge permanently are almost invariably branches on the same side as the obstruction—*e.g.*, the *right* inferior thyroid and vertebral arteries dilate after ligature of the *right* carotid. The primary anæmia, the blush and heightened temperature of vascular dilatation, and the final return to the normal, can be seen in limbs after ligature of main vessels (p. 240).

HYPERÆMIA.

Hyperæmia, or **congestion**, is excess of blood in the more or less dilated vessels of a part. It may be (1) **active** (**arterial**) or (2) **mechanical** (**venous**). These two varieties must be considered separately.

ACTIVE OR ARTERIAL HYPERÆMIA.

Active hyperæmia means excess of arterial blood in a part, with, in most cases, acceleration of flow.

CAUSES.—The immediate cause of active hyperæmia is in all cases **diminished arterial resistance.**

Diminished arterial resistance may be produced pathologically :—

1st. **By certain agencies which have a weakening or**

paralysing effect upon the involuntary muscle of vessel-walls. *Fatigue* from previous prolonged contraction has this effect, as seen in the hyperæmia of the hands which follows snowballing. Warmth, too, is generally placed under this heading. *Injuries* of all kinds, when not acting suddenly and with extreme severity, produce a reflex hyperæmia by their influence on sensory nerves. This occurs before the *true* inflammatory dilatation sets in, and must be included in the next group of cases. The dilatation *characteristic* of *inflammation* is due to direct damage of the vessel-wall, and therefore falls under this heading; and, so long as it is more than sufficient to counterbalance the increased resistance which always accompanies it (see "Inflammation"), the quantity of blood passing through the part is greater than normal—*i.e.*, the part is hyperæmic. The *sudden removal of pressure* is another cause of hyperæmia. Thus, congestion of the abdominal vessels follows the removal of much ascitic fluid, or of a large ovarian tumour: bleeding from the pleura occurs when the cavity is rapidly emptied by aspiration or strong syphon-action: bleeding may also follow the complete emptying of a chronically distended bladder. The muscle of the vessels, accustomed to much support, has lost power; so, when the support is suddenly removed, the vessels dilate fully, and small ones perhaps rupture.

2nd. **By the removal, either directly, or reflexly**—*i.e.*, **by inhibition—of the vaso-tonic action of the sympathetic.** Thus, active congestion follows pressure upon the sympathetic—as in the neck—by an aneurysm. Certain drugs, taken internally, are believed to directly paralyse the vaso-tonic nerves—*e.g.*, nitrite of amyl, alcohol, tobacco.

The *reflex* process is generally due to stimulation of sensory nerves, the diminution in tonus thus produced being more or less accurately confined to the region supplied by the nerve. Friction and slight irritants in the early stages of their action produce hyperæmia in this way (see above). It seems that vascular dilatation of deep organs may be produced reflexly by the application of stupes to the skin over them.

Anæmia of any large part—as of a limb, compressed by Esmarch's bandage, or of the skin from cold—necessarily causes *hyperæmia* of other parts—**compensatory hyperæmia.** But all parts do not suffer equally, as they would do were the hyperæmia the result simply of increased arterial pressure; certain vessels, as the great abdominal veins, dilate, showing that the vaso-motor system arranges for the

accommodation of the surplus blood by producing local diminutions of vascular resistance. After extirpation of one kidney, its share of blood passes mainly to the other.

3rd. **By excitation of vaso-dilator nerves,** such as the chorda tympani. Nothing is certainly known of this as a cause of hyperæmia; but the hyperæmia associated with facial neuralgia and that of the thyroid in exopthalmic goître, have been referred to vaso-dilator neuroses, and also to inhibition of vaso-tonic nerves.

RESULTS.—The results of active hyperæmia are principally such as might be expected from increase in the amount of arterial blood, and in the rapidity of its flow, in any particular organ or tissue. The symptoms in a superficial part are—increased redness and pulsation, a subjective sensation of throbbing, some increase in bulk, and marked elevation of surface temperature, until this approaches that of internal organs. If the hyperæmia be of long duration, or frequently repeated, the small arteries remain permanently enlarged, their walls gradually thicken, and the epithelium and connective-tissues of the part increase. This may be seen in the papillary thickening round a callous ulcer of the leg, and the occasional spread of ossification from the tibia into the granulation-tissue. The ability to work is increased, and hypertrophy will follow if the increased work is maintained (p. 96). In hyperæmia of the nervous centres, we see great excitability, paræsthesiæ of sight and hearing, and even convulsions. In some glands, such as the kidneys, secretion is increased, the urine being watery and sometimes albuminous.

MECHANICAL OR VENOUS HYPERÆMIA.

In venous hyperæmia, the excess of blood is in the veins and capillaries, and the flow, instead of being accelerated, is retarded. This is so frequently produced by some obvious mechanical obstacle to the return of blood through the veins, that it is often called **mechanical** hyperæmia. The congestion of a finger, produced by a moderately tight band tied round it, may be taken as the type of such cases.

CAUSES.—Anything which weakens the forces carrying on the venous circulation, or which opposes unusual resistance to this circulation—must tend to produce venous hyperæmia. Such

causes may exist in any part of the vascular system—heart, arteries, capillaries, or veins—some having a local, others a general effect. They may be arranged under two headings—(1) those which *diminish* the *vis a tergo,* or propelling force; and (2) those which *introduce* a *vis a fronte,* thus placing a direct impediment to the return of blood by the veins.

1. Chief in the first group is **diminished cardiac power.** The heart may act so feebly or be so damaged structurally (see "Endocarditis"), that too little blood enters the arteries at each stroke, and generally at a pressure less than normal. As a result the arterial supply of all parts is diminished, blood lags in the veins, and a less quantity than normal returns to the heart during each diastole. This is very evident in prolonged febrile diseases, such as typhoid, and in those degenerations of the walls of the heart, which lead to dilatation of its cavities. In whichever of these ways the *vis a tergo* is diminished, that diminished fulness of the arteries and over-fulness of the veins, which are so familiar clinically as the result of **cardiac failure,** will be produced. If this condition be of long duration, there is necessarily so much interference with the oxygenation of the blood, with the functions of the blood-forming organs, and with the processes of digestion and assimilation, that the blood itself becomes deteriorated, and thus by its lagging in every tissue the nutrition of all suffers.

In the arteries the driving force may be weakened (1) by total or partial *obstruction* of an arterial trunk; (2) by *dilatation,* arising from simple atony, or from those general fatty, atheromatous, or fibroid changes of the arterial wall, so common in advanced life; or (3) by *rigidity,* in which case, owing to loss of arterial elasticity, the heart's force is wasted against the walls of rigid arteries.

Obstruction to the circulation **in capillaries** arises mainly from pressure of inflammatory and serous effusions on capillary areas.

With regard to **veins** the circulation will be slowed by (1) absence of muscular contractions, especially in the lower extremity; (2) such dilatation as produces incompetence of valves, thus rendering muscular action useless as an aid to circulation; and (3) by anything which, diminishing the elastic force with which the lung tends to draw away from the pleural-wall, lessens thoracic aspiration. Forcible expiration will replace the normal *minus*-pressure within the thorax by a *plus*-pressure: thus playing wind instruments impedes entry of blood from veins into the heart. Emphysema, effusion of air or fluid into the

pleural cavities, and large new growths of the lung act similarly. These causes might fairly rank under the second heading.

When, by various combinations of the above conditions, the circulation is much retarded, **hypostatic congestion** occurs. The commonest seats of this are the posterior edges and bases of the lungs, the skin over the sacrum, and any parts kept constantly dependent. Slowing of the circulation causes distension of the veins and increase of the intravenous pressure. In any such part which is also dependent, the intravenous, and therefore capillary, pressure is further increased by *gravity*. The force of gravity is in proportion to the vertical distance between the highest point of the body for the time being, and the part in question. If the patient is so weak as to be unable to change his position, this pressure constantly acts upon the same veins and capillaries, dilating them, and greatly increasing the tendency to leakage through their badly nourished walls. Thus the part is redder and softer than normal, and is œdematous (p. 221). In bedridden patients breathing is often very shallow, and the effect of expiration in driving blood on to the left auricle is therefore diminished (see "Hypostatic Pneumonia"). In people, who are walking about, dropsy from heart-disease generally begins in the legs. This is due largely to the action of gravity.

2. Examples of direct impediments to the return of blood by the veins are numerous. Thus, congestion of the chylopoietic viscera from compression of the portal capillaries occurs in cirrhosis of the liver; congestion of the lung follows mitral constriction or regurgitation; congestion of the systemic circulation results from insufficiency of the tricuspid valve; and in the lower extremities the same result may be due to pressure of the gravid uterus on the iliac veins.

RESULTS.—Whether there be a direct impediment to the return of blood by the veins, or a failure in the forces of circulation, the veins and capillaries dilate, and the blood, moving with diminished velocity, accumulates in them. The subsequent changes will depend upon the degree of obstruction to the venous return, and upon the arterial pressure; in other words, upon the injury sustained by the vessel-walls from impaired nutrition, and upon the increase of pressure in the veins and capillaries. In addition to the immediate effects, such as the diminished secretion of urine, the most important of the more gradually induced changes are the exudation of serum, the escape of red blood-corpuscles, hæmorrhage, fibroid induration, thrombosis, and necrosis.

1. **Exudation of Serum** is one of the most important results of mechanical hyperæmia. It is discussed on p. 219.

2. **Escape of Red Blood-corpuscles** occurs when obstruction to the venous return is very great: they transude with the fluid from the veins and capillaries. The blood-stream in these vessels completely stagnates, and the red corpuscles become packed into a coherent mass which oscillates to and fro with the arterial pulsation. Then, suddenly, some of the red corpuscles penetrate the walls of the small veins and capillaries and escape into the surrounding tissues. This seems to occur without rupture of the vessel, for if the ligature be removed, the blood again circulates in a perfectly normal manner. The corpuscles rarely escape in great numbers. It has been suggested that they pass through the stomata which Recklinghausen has shown to exist between the endothelial elements; but as plasma could easily pass through openings large enough for a red corpuscle, and as the transudation-fluid differs markedly from plasma, Cohnheim considered that the existence of these stomata is unnecessary to account for the escape of corpuscles.

3. **Hæmorrhage** is another result of mechanical hyperæmia, and usually occurs only when the obstruction to the venous current is very great, and when the nutrition of vessels and tissues has suffered from long congestion. Healthy vessels can bear very heavy strains without giving way. Those vessels which are the least supported are the first to give way. Hæmorrhage into the stomach in cirrhosis of the liver, and into the lung in mitral stenosis are familiar examples of this result.

4. **Fibroid Induration** is due to a gradual increase in the connective-tissue round the blood-vessels, and is one of the most important results of long-continued mechanical hyperæmia. The interstitial growth was formerly supposed to lead to atrophy of the higher structures, and thus to impairment of the functions of the organ. In the stomach, it was said to produce atrophy of the glandular structures; in the kidney, compression of the urine-tubes; and, in the heart, diminution in motor power. It is probable, however, that the atrophy in these cases is primary, following the deficient supply of oxygenated blood, and that the increase in the stroma is due to the fact that it is the only tissue present that can thrive on the material supplied. The alterations which this change produces in the physical characters of the organs—viz., induration associated with abnormal redness, due to the excess of blood or pigmentation from hæmatoidin—are exceedingly characteristic.

5. **Thrombosis** (see p. 223).

6. **Necrosis** occurs from mechanical hyperæmia only when the obstruction is very general and complete (pp. 19, 22 and 28).

To sum up, long-continued mechanical hyperæmia leads to impairment of vitality and function. The tissues gradually undergo retrogressive changes and atrophy, although from the amount of exudation and blood which they contain, their size and absolute weight may be increased. This form of hyperæmia has no tendency to cause multiplication of tissues other than of the *connective,* and, in the case of catarrhs of mucous membranes, of the *epithelial.*

POST-MORTEM EVIDENCES OF HYPERÆMIA.—Parts which were actively hyperæmic during life frequently show no signs of it after death : for, if coagulation does not occur immediately, contraction of the arteries or of the elastic capsules of organs forces the blood on into the veins, thus rendering the recognition of arterial or capillary hyperæmia impossible. Further, under the influence of gravity alone, fluid blood will tend to run to the more dependent parts : and thus a hyperæmic organ—whether actively or passively so—may be emptied of blood and may thus appear pale.

But dependent parts, on the other hand—the posterior portions of the lungs, the lowest coils of intestine, the skin on the posterior surface in dorsal decubitus—which may have been healthy during life, now become full of dark blood. It is often difficult to say how much of the congestion of the base of a lung is ante-mortem and how much post-mortem.

A further source of error exists in the post-mortem staining of parts, especially of the endocardium, the linings of great vessels, and the tissues round veins, such as is met with, particularly in septicæmia. The redness in these cases is *uniform,* and no magnification will show that it depends upon distended vessels, while a simple lens will generally show the capillary nature even of an apparently uniform *hyperæmic* redness.

When large veins are hyperæmic, the injection is said to be "ramiform," from their branching form and dark-blue colour. In the intestine, skin, and kidney, hyperæmia may appear punctiform from the arrangement of the vessels in villi, papillæ, or Malpighian corpuscles as the case may be. Minute punctiform hæmorrhages must not be mistaken for such cases.

Pigmentation (slate-grey, black or brown) from the altered hæmoglobin of disintegrated corpuscles generally remains after chronic

hyperæmia, as is often seen in the stomach and intestines after portal congestion, and in the bladder and the lungs after chronic catarrh (p. 218).

Mechanical Hyperæmia of the Liver.

Long-continued mechanical hyperæmia of the liver invariably gives rise to the condition known as **Nutmeg Liver,** which so frequently results from cardiac incompetence. The change is charac-



FIG. 91.—*Nutmeg Liver.* Destruction of the liver-cells and pigmentation of the central portions of the acinus; new growth of connective-tissue at the periphery. V. Hepatic vein. P. Portal canal. × 50. When more highly magnified, numerous nuclei are seen in the peripheral connective-tissue. In this specimen there is more new tissue at the periphery than is usual.

terised by a large accumulation of blood in the sublobular and intralobular veins, which dilate and thicken; by atrophy of the hepatic cells in the central portions of the lobules; and rarely by increase of the interlobular connective-tissue. The impediment to the return of blood by the hepatic veins leads to atrophy of the cells in the central portions of the acini and to the deposit of pigment, so that, when examined microscopically, these portions of the acini are seen to consist of broken-down cells and granules of pigment (Fig. 91). The

intralobular veins and their radicles are much dilated, and filled with red blood-corpuscles (Fig. 92). Their walls are thickened, and there often appears to be also more or less thickening of the intercellular network which immediately surrounds the central vein. Owing to this thickening of the central vein and of the adjacent intercellular network, and to the destruction of the liver-cells, the most central portions of the acini, in advanced stages of the disease, may present a fibrous appearance. This appearance is much less marked in injected specimens, and is therefore chiefly due to atrophy of the cells and distension of the vessels. At the peripheral parts of the acini new

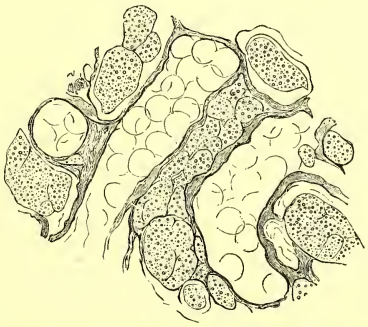


FIG. 92.—*Nutmeg Liver.* Portion of Fig. 91, near central hepatic vein (V), more highly magnified. Showing the thickening of the veins, and the accumulation of red blood-corpuscles within them. × 400.

interlobular growth is occasionally seen insinuating itself between the almost unaltered liver-cells. This new interlobular growth is less nucleated than that met with in cirrhosis of the liver.

In the earlier stages of this affection the liver is smooth and often considerably increased in size from the large amount of blood which it contains. On section, it presents a peculiar mottled appearance, the centre of the lobules being of a dark-red colour, whilst the peripheral portions are of a yellowish-white. This latter appearance is occasionally increased by fatty infiltration of the peripheral liver-cells. The appearance of such a section is not unlike that of a nutmeg. Ultimately, the organ may undergo a gradual diminution in size, becoming more or less irregular on the surface. This is due to atrophy of the central cells of the lobules mainly from mal-nutrition (p. 214), but partly from pressure of the dilated central veins and the contracting interlobular growth.

Mechanical Hyperæmia of the Lungs.

In the lungs, long-continued mechanical hyperæmia produces that peculiar induration and pigmentation which is known as **Brown Induration**. This most frequently results from stenosis and insufficiency of the mitral orifice. The alterations produced in the pulmonary texture consist in the first place of elongation and dilatation of the pulmonary capillaries, so that even in uninjected preparations the alveolar walls appear abnormally tortuous. The epithelial cells lining



FIG. 93.—*Brown Induration of the Lung.* Showing the abnormal number of swollen pigmented epithelial cells covering the alveolar walls, the increase of connective-tissue around the blood-vessels, *a*, and the large quantity of pigment. *b*. The alveolar cavity. × 200.

the alveoli become swollen, probably multiply, and are seen in large numbers, filled with dark-brown pigment, covering the alveolar walls (Fig. 93). They frequently accumulate within the alveolar cavities. These changes are followed by an increase in the interlobular connective-tissue, by the formation of large quantities of brownish-black pigment, and often by a thickening of the alveolar walls. The bronchial mucous membrane is dark and the small peribronchial vessels are dilated. Sometimes these vessels rupture and blood is extravasated into the tissue of the lung (see "Pulmonary Apoplexy").

Lungs, in which these changes are at all advanced, present a more or less uniform brownish-red tint, mottled with brown or blackish-coloured specks and streaks. They are heavier and tougher than

natural, less crepitant, and upon squeezing them the pulmonary tissue is found to be denser and thicker than that of a healthy lung.

DROPSY.

The normal tissues are continuously bathed in, and nourished by, the lymph, which derives its nutritive properties from the blood, and passes on into that fluid the products it receives in exchange from the tissues. These products find their way, either by the veins or by the lymphatics, back to the heart, and thence to the lungs, skin and kidneys. In all probability the veins are quite as much the soil-pipes of the tissues as the lymphatics. To describe in all parts of the body a constant circulation of lymph transuding from the capillaries and returning by the lymphatics, is more than is justified by our present knowledge. In the dog, at any rate, we know that during rest there is no flow at all from the lymphatics of the limbs. The lymphatics seem to perform most of their work during active exercise, or in other local emergencies.

Lymph varies both in amount and in composition. The two factors which are mainly operative in determining these are—(1) the excess of the pressure within the capillaries over that in the tissues immediately around them; and (2) the special properties of the cells of the capillary walls.

1. The **capillary pressure** is, in general terms, a sort of resultant between the arterial and venous pressure. It usually follows most closely that in the veins. If either the arterial or the venous pressure rise or fall, while the corresponding venous or arterial pressure remains *constant,* the capillary pressure will rise or fall too, as the case may be. If, however, one of them, either the arterial or the venous pressure, rise or fall while the other moves in a *contrary* direction, the resulting capillary pressure may rise, remain constant, or fall. Under such circumstances the capillary pressure is difficult to estimate, for there is no method of direct measurement. Most often, as has been said, it follows that in the veins. A statement regarding the arterial pressure alone is rarely a safe guide to that in the capillaries, partly for the reason just stated, and partly because the arterioles may interpose an additional indeterminable factor.

2. The influence exercised by the **capillary walls** upon the production of lymph has been supposed by Heidenhain and others to be of the nature of an active secretory process, but by many it is still

regarded as a passive factor, the efficacy of which depends only on the efficient nutrition of the vessel-walls. According to this second view, a vessel-wall is said to be more or less "permeable" in proportion to (1) the readiness with which it allows fluid to transude (sensitiveness to pressure); and (2) the resemblance which the transuded fluid bears to the plasma of the blood. Thus, so long as the pressure remains constant, the *permeability of the capillaries* is the measure of both the amount and the composition of the lymph. For example, the capillaries of the liver are said to be more permeable than those of the intestine, and those of the intestine than those of the limbs. By this is meant that a similar increase of pressure induced in each case will not be followed by a similar result, but that there will be a marked increase of the lymph-flow from the liver, a less increase from the intestines, and the smallest increase of all from the limbs; and that in any case the lymph from the liver will contain more proteid matter than that from the intestines, and that from the intestines more than that from the limbs. The saline constituents are the same in all cases, and correspond in amount to that found in the blood-plasma. It is well-known that ascitic fluid contains more albumin than œdematous fluid from the legs, and that this is so under all conditions, and does not depend on the disease producing the dropsy. *Damage*—such as dipping a limb into very hot water—increases the permeability of the capillaries, and therefore both the amount of fluid transuded and the resemblance which it bears to blood-plasma. It is probable that a somewhat similar but less pronounced change may be caused by gradual alterations in nutrition, due to the circulation of defective or vitiated blood, and that increased friction and greater permeability may result.

Heidenhain found that by introducing certain substances into the blood he could produce an increase in the flow of lymph. These substances he called "lymphagogues" believing that they in some way stimulated the supposed secretory power of the capillary walls. Starling* has, however, by very ingeniously contrived experiments, shown that, in the case of dextrose, the first effect of its introduction is to cause a reabsorption of fluid into the vessels, and a consequent increase in the total quantity of fluid they contain. This, in its turn, produces a rise in the venous, and therefore in the capillary pressure; and to this increased pressure, rather than to any special secretory process, he attributes the additional lymph-flow. Starling further shows that if an amount of blood equal to the expected

* *Journal of Physiology*, 1894.

absorption—caused by the introduction of the dextrose—be previously withdrawn, no increase in the total amount of blood, no rise of the venous pressure, and no addition to the ordinary lymph-flow, will occur. It seems therefore that *permeability* should still be regarded as the possession of a special power of retention rather than as an active secretory process.

By **dropsy** is meant the retention of lymph, either in connective-tissue spaces or in serous cavities, though by some it is used only with reference to the serous cavities. The term **œdema** is limited to dropsy of the connective-tissue spaces, while **anasarca** means œdema of the subcutaneous tissue. Thus we speak of "general dropsy," "œdema of the lungs," "anasarca of the legs."

It is tolerably certain that the causes of increased lymph-flow are also the causes of dropsy. It is quite certain that the most marked examples of dropsy are, in practice, associated with **enormous increase in venous pressure** acting over a long period. Among these, *local obstruction* to the return of venous blood plays the chief part. This may be caused by the pressure of cicatricial tissue, or a tumour, or by thrombosis. *Inefficient action of the heart,* such as that occurring in late stages of valvular disease, causes a fall in arterial but a rise in venous pressure, with a consequent slowing of the circulation. As the veins become distended their valves become incompetent, and the action of gravity on the enlarged blood-column adds enormously to the pressure in the capillaries of the legs, and thus produces anasarca. A slighter form of œdema of the legs, in women whose occupation involves much standing, is due to the combined influence of constipation, garters, and gravity. In all these cases the mechanical congestion may not improbably increase the *permeability* of the capillary walls. The certainty that the increased venous pressure is the cause of the dropsy, rests mainly on the constancy with which the dropsy disappears when the increase in pressure is removed. *Increased arterial pressure* is sometimes credited with the production of dropsy, but it is uncertain whether, in the absence of increased venous pressure, it is a sufficient cause. In that form of chronic Bright's disease, known as granular kidney, there is a marked increase in the arterial pressure, but no œdema until the heart's action begins to fail, and the venous pressure consequently rises. Possibly in such conditions the contracted arterioles may partially neutralise the effect and act as a guard to the capillaries. An experiment of Heidenhain's shows how fallacious it is to trust to arterial

pressure as a guide to that in the capillaries. By obstructing the thoracic aorta this observer enormously reduced the arterial pressure. Notwithstanding this reduction, he found that the combined lymph-flow from the intestines and liver together showed no proportional fall, though the lymph obtained included an appreciably larger amount of proteids. Heidenhain's inference was that no process of mere tissue-filtration could possibly explain the result. Starling repeated this experiment, but took the precaution of measuring the pressures in the portal vein and in the inferior vena cava, as well as in the femoral artery. He found that the enormous fall in the arterial pressure was accompanied by a considerable *drop* in that in the portal vein, but by a distinct *rise* in that in the inferior vena cava; so that, though the pressure in the intestinal capillaries was almost *nil*, the pressure in those of the liver was probably *increased*. He further showed that the flow of lymph from the intestines ceased, while that from the liver (normally the more concentrated) continued, as might have been inferred from the pressure conditions. In this way the changes in capillary pressure were found to explain the alterations in both the quantity and character of the lymph.

The second great class of dropsies are those associated with **inflammation of the kidneys** and deficient urinary secretion. In these cases there is no ascertained increase of venous pressure. It is true that the pressure in the arteries is often raised, but the rise bears no uniform relation to the œdema. It has been suggested that in these cases there are substances circulating in the blood, acting like the experimentally injected dextrose, and that these substances produce a condition of plethoric hydræmia and a consequent general rise of blood pressure, followed by œdema. Against this view it may be urged that in the experiment referred to, the increased flow affects only the abdominal viscera, whereas the œdema in Bright's disease is distributed over all the loose tissues on the surface of the body. We know, however, practically, that improvement in the quality of the blood is followed by diminution in the amount of œdema.

In cardiac failure there must be some hindrance to the exit of lymph from the thoracic duct, and this may be an adjunct in dropsy due to cardiac causes. Local pressure on the lymphatics does not usually produce œdema, though the occasional presence of chyle in the urine, or in the pleural or peritoneal cavities, is generally attributed to blocking of the respective lymphatics by growths or parasites, or to rupture of the thoracic duct or receptaculum chyli.

In anæmia, neuralgia, exophthalmic goître, tumours of the spinal cord, and other diseases, slight degrees of œdema are occasionally met with. Section of the spinal cord produces vaso-constrictor paralysis, and tumours probably act in a similar manner. In the other cases vaso-motor derangements are common, and though their cause is less definitely ascertained, paralysis of vaso-constrictor, or direct action of vaso-dilator nerves is probable, and would furnish a sufficient cause. Experimental anæmia gives rise to no increased lymph flow, but it does not follow that defective blood acting over a long period might not increase the permeability of the capillaries. Experiments on the spinal cord, and on the splanchnic and vagus nerves have hitherto failed to afford satisfactory evidence of the existence of any nervous cause of œdema *apart from* vaso-motor changes.

THROMBOSIS.

Thrombosis is the coagulation of the blood within the vessels during life. The product is called a **thrombus**, in opposition to a **coagulum** or **clot**—the result of post-mortem coagulation. Thrombosis may occur in the heart, arteries, capillaries or *veins*. It is in the *veins* that it most frequently occurs.

CAUSATION.—Thrombosis is generally said to be due to one or more of three causes: damage or absence of the lining of the vessel-walls, retardation of the blood-stream, and changes in the blood itself increasing its coagulability. These causes we shall now proceed to discuss.

I. **Damage or absence of the lining of the vessel-wall.**—The most striking points are, first, that blood, circulating in living vessels, remains fluid, while blood drawn from the body coagulates; and secondly, that when coagulation of circulating blood occurs, it is usually upon some obviously diseased surface, or in some place where the blood-stream has been much retarded. From these facts it has been inferred that the healthy vessel-wall exercises an inhibitory influence upon the coagulation of the blood, preventing the changes (whatever they may be) which lead to the formation of fibrin. It is probably more correct to say, with Lister, that blood within normal vessels does not tend to coagulate, the vessel-wall being, so to speak, neutral or passive so long as it is living and healthy. In this light the normal vessel-wall may be compared to greasy and viscous substances,

like vaseline, paraffin and castor oil, in which blood may long be kept fluid, and yet be ready to coagulate normally as soon as it is brought into contact with solid matter. Contact with ordinary solid matter, on the other hand, induces coagulation more or less quickly. When drawn into a basin, blood usually clots in from three to eight minutes, but Lister saw blood remain fluid for a long time in the angle between an amputated sheep's foot and the skin raised in a flap from it. Moreover, extravasations about simple fractures and into the cavities of the body are often long in coagulating, though they vary much in this respect. Coagulation occurs more rapidly on a rough surface than on a smooth surface.

Although the integrity of the *vessel-wall* has been spoken of, the integrity of the *endothelium* is alone necessary. Fatty and calcareous changes of the deeper structures do not cause thrombosis, whilst atheromatous ulcers, foreign bodies, and nodules of new growths—all bare of endothelium—may; moreover, severe injury of capillaries, which possess only endothelium, causes thrombosis in them. It may therefore be concluded that *damage* or *absence* of the vascular endothelium is an essential condition in the production of thrombosis. This damage or absence, as already stated, may be due to many causes.

1. **Injuries** *may destroy or injure the endothelium.* Among the most important of these are section, rupture, ligature, and torsion of vessels. In section and rupture, thrombosis starts from the damaged intima and constitutes the means by which hæmorrhage is naturally and temporarily arrested. By ligature, torsion and other operative proceedings surgeons can also temporarily arrest hæmorrhage which the natural processes are insufficient to stop. Cauteries and caustics furnish other examples of the effect of injury in producing thrombosis.

2. **Diseases** *of the vessel-walls may affect the endothelium.* Thus thrombosis may occur on atheromatous ulcers, bare calcareous plates, or an intima damaged by syphilitic inflammation, or by the extension of spreading inflammations from other parts. Inflammation was formerly regarded as the main, if not the only, cause of thrombosis; hence thrombosis in veins is frequently termed "phlebitis" even at the present day. Inflammation of veins is rare as a *primary* condition, but it may be due to extension of inflammation from neighbouring tissues, and not infrequently *results from* the formation of a thrombus.

The thrombosis which occurs as an occasional complication of acute specific fevers is explained by the observation of Ponfick that in these

diseases desquamation of endothelium may occur over large areas of vessels.

In the heart, inflammation of the endocardium causes destruction of its endothelium, followed by the growth of granulation-tissue on the opposed surfaces of the valves: thrombosis frequently occurs upon these vegetations (see "Endocarditis").

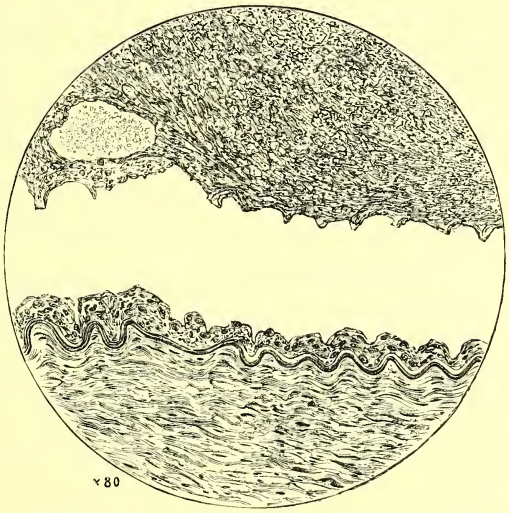


FIG. 94.—Section of a thrombosed popliteal artery, a fortnight after ligature, showing persistence of almost the whole of the intima. The thrombus has been torn from the vessel-wall. (Mott.)

3. **Imperfect blood supply** *of a part, causing disease of the vessel-walls by imperfect nutrition.* Here slowing of the circulation is the indirect, and deficient vascular supply the immediate cause. It is probably not a very important group, as there are reasons for supposing the nutrition of the vessel-wall depends on the circulation in the vasa vasorum, and not on that in the affected vessel (Fig. 94; see "Inflammation of Arteries"), and there is no necessary relationship between these two portions of the circulation. This cause is chiefly operative in the case of the smallest vessels. The conditions affecting the blood-supply will be considered in a subsequent section.

4. *The* **presence** *in the vascular system of* **substances** *not covered by*

endothelium. These comprise such things as needles, horsehair, or wire introduced into the sac of an aneurysm; pre-existing clots (thrombi or emboli); parasites which have penetrated the vessels; and new growths which project into the interior of veins. In all these instances the clotting first takes place upon the foreign substance itself.

II. **Retardation of the blood-stream.**—Sometimes abnormality of surface is insufficient to cause extensive clotting, until retardation of the blood-stream is added. For example, in the aorta we sometimes find calcareous plates uncovered by endothelium, but with little or no adherent fibrin. In aneurysms, too, the wall is always abnormal and the circulation somewhat retarded; but sufficient clotting to effect a cure may not occur until, by treatment, we still further reduce the current, and thus prolong the contact of the blood with the abnormal surface.

On the other hand, retardation, or even arrest, seems quite unable by itself to produce thrombosis. So long as the endothelium is kept fairly nourished within the vessel, the stagnant blood will not coagulate. Blood within a tied-off turtle's heart does not coagulate until the heart dies. The time preceding the occurrence of coagulation in the jugular vein of a mammal is longer in proportion to the care exercised in laying it bare and applying the ligatures; and if this operation be done antiseptically, coagulation may not occur at all.

How are these very different results to be explained? Impaired circulation in a part means damage to all the tissues supplied—to the vascular endothelium among others. It is of course possible that diminishing the rapidity of the blood-stream may have no other influence than that which it exerts in this direction. There are, however, reasons for assigning to it a more direct action. All parts of a stream flowing through a tube do not proceed at the same rate. The central or axial part of the stream invariably travels faster than the peripheral or periaxial, for it is exposed to less friction. If solid particles be suspended in such a fluid, those with a specific gravity most closely approaching that of the fluid will move most rapidly, and maintain their position in the axial stream most easily. If the rate of flow be diminished, the tendency of the suspended particles to remain in the axial stream will also diminish, and this will be in proportion to the difference between their respective specific gravities and that of the fluid in which they are suspended.

In most arteries and in many veins the periaxial stream contains only

plasma and a few leucocytes. But directly the stream slackens, the leucocytes fall out more rapidly than ever and lag behind close to the walls, while even the red corpuscles maintain less perfectly their axial position. The blood-platelets (blood-plates, hæmatoblasts) generally occupy the axial stream, but fall out soon after, and from the same cause as the leucocytes. Now whether we attribute to the leucocytes or to the platelets the chief function in the production of the thrombus (p. 229), it is quite evident that, though the lining membrane of the vessel be diseased, yet the increased friction thereby produced may be insufficient to cause any practical slowing of the blood-stream at that point, and insufficient therefore to bring either platelets or leucocytes into contact with the damaged part of the wall. In this way we may have an abnormal endothelial lining without any resulting thrombosis.

On the other hand, when the current is slow, as in the veins, the leucocytes and platelets will readily come into contact with the sides of the vessel and may produce clotting, even though the damage to the vessel-wall be comparatively slight. In this way we find that neither damage to the endothelium nor slowing of the circulation need be followed by thrombosis; and that the former is the more important cause of the two, because there are many places where the blood-stream is naturally slow.

A tendency to stagnation of blood may be due to many causes, of which the most important are cardiac weakness, general diminution of vascular tonus, and dilatation (varix) of veins. All these may well be combined in a single case to retard the circulation, and thus to produce an abnormal vessel-wall and prolonged contact of the same blood with it. They are the conditions which give rise to the "marasmic clots" of Virchow. These form *in the most dependent veins—e.g.,* those of the lower limb, pelvis, or back; *in the cerebral veins and sinuses,* where the venous circulation is ordinarily very slow and difficult; and *in* those *parts of the heart* in which blood tends to remain when the organ first fails to contract efficiently—*e.g.,* the auricular appendices, the apices of the ventricles, and the spaces between the trabeculæ. In veins these clots begin just behind the flaps of valves. The force of the venous current is so slight, or the resistance to it so great, that it no longer opens the valves completely; the blood consequently stagnates, and, after a time, coagulates behind the cusps. Such clots occur in the course of many exhausting diseases—as phthisis and cancer—in which thrombosis is materially facilitated by the quiescent state of the

patient. Careful examination of the sites of recent thrombi is said to have demonstrated absence of endothelium, but this is hardly proof that alteration of the endothelium was the cause of the thrombosis, for the cells may have disappeared secondarily.

In varicose veins, which are frequently the seats of thrombosis, the circulation is extremely slow, and the endothelium, owing to imperfect nutrition, can scarcely ever be healthy, though it is not always so damaged as so excite coagulation.

III. **Certain conditions of the blood** favour coagulation and promote the occurrence of thrombosis. It is said that the tendency to coagulation is increased during the later months of pregnancy, after profuse hæmorrhage, and in certain acute inflammatory diseases, such as acute rheumatism, erysipelas, pneumonia and pleurisy. To whatever cause it may be due, an increased tendency of the blood to coagulate is probably never more than a predisposing cause of thrombosis. In septic fevers, thrombosis is not uncommon in places having no direct relation to a wound. This has been attributed to the breaking up of leucocytes in large numbers; for it has been shown that injection of leucocytes into the circulation of animals is followed by their rapid disintegration and local or even general thrombosis. In all these diseases a failing heart and flagging circulation—the causes of ordinary marasmic clotting—are present. Perhaps desquamation of endothelium (p. 224) occurs; and it is possible that organisms may play a part in the process. The presence of organisms seems particularly likely in those frequent cases of venous thrombosis, often going on to puriform softening and secondary phlebitis, which occur side by side with erysipelas, and pyæmia, and which have gained for "phlebitis" a place amongst "hospital" diseases.

It is well known that the presence of calcium salts is essential to the coagulation of the blood, while the addition of oxalates will neutralise the effect of their presence and prevent coagulation. So also, among the products of cell-action, substances allied to nuclein aid coagulation, while albumoses hinder it. We do not yet know the bearing of these facts upon the phenomena of thrombosis.

CHARACTERS OF CLOTS AND THROMBI.—Post-mortem coagula in the heart are generally *buffy*. The thickness of the pale layer varies directly with the time which elapses before the changes in the heart-substance allow coagulation to begin; while its position indicates the part that was uppermost after death.

Post-mortem clots are red, soft, watery and never adherent. They do not *fill* the vessels, and can be easily drawn out of them as long strings.

Clots formed in the heart just before death differ somewhat from the preceding. They are partly due to the "whipping" of the blood by the chordæ tendineæ and other structures. They occur in cases of slow death, when the heart is too weak to empty its cavities, and the blood tends to stagnate. As would be expected, they are more or less uniformly decolorised, and, though not adherent, are often so much entangled among the chordæ and trabeculæ, that they cannot readily be removed. From their longer duration and more complete contraction, they are firmer and tougher than true post-mortem clots.

Thrombi or ante-mortem clots are of two kinds—**red** and **white**, according as they originate from *quiescent* or *circulating* blood. In the former case, as seen in an artery or vein after ligature, more or less of the stagnant blood on either side of the knot coagulates into an ordinary **red** clot—soft, uniform on section, and adherent to the vessel-wall where this is injured. The thrombus, still adhering to the wall, then contracts, becomes drier and less elastic, but still remains red. This is the state in which a red thrombus is generally found.

But, when coagulation occurs in blood *which is still circulating*, as in the sac of an aneurysm or on a cardiac vegetation, a **white** or **mixed** thrombus results. Zahn studied the formation of such clots in small veins, irritated by a small crystal of salt in their neighbourhood. According to this observer, the abnormal surface causes each successive quantity of blood which passes to leave upon it a little fibrin and some leucocytes; whilst, if the blood-stream is languid, some red corpuscles remain in the thrombus, rendering it mixed. But later observers have shown that innumerable blood-platelets and not leucocytes are deposited upon a thread passed through a vessel, and also, in the case of a severed artery, upon the adventitia within which the cut vessel has retracted. Moreover, an examination of old clots in aneurysms has convinced Osler that they, too, consist of platelets, and he, consequently, regards leucocytes as of little importance in the formation of thrombi (p. 227). These thrombi are *greyish-white or reddish, firmly adherent to the wall, and it is peculiar to them that they are often stratified.* This is probably due to variations in the rate of deposition of the fibrin, in the blood-pressure to which it is subjected,

and in other physical conditions. Frequently white and reddish layers alternate.

A thrombus may be "parietal" or "obstructive," causing partial or complete occlusion of the vessel. Once formed, it extends by deposition of more fibrin on its surface. As a rule, this extension is checked by the rapidity of the blood-current at the junction of the first large collateral branch in each direction; but sometimes, especially in veins, thrombosis becomes "continued," and a clot may extend from the foot to the vena cava. Both in arteries and veins, extension is most likely to take place toward the heart, though it may occur in an opposite direction. These thrombi generally adhere to the wall throughout

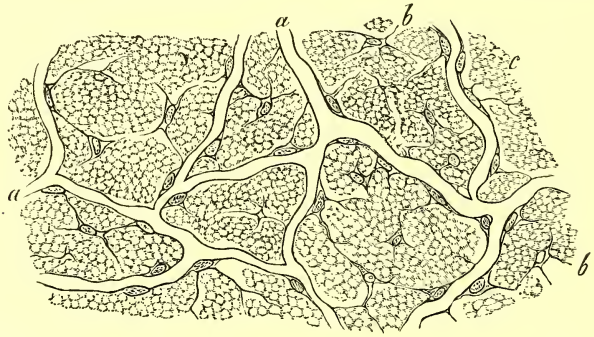


FIG. 95. — *Section of an Arterial Thrombus thirty-seven days old.* *a*. New blood-vessels. *b*. Leucocytes and anastomosing cells. (Rindfleisch.)

their whole length, but sometimes they do so only at their points of origin.

In the capillaries, coagulation occurs only as a result of necrosis or grave injury of the capillary-walls; for they are so small that, so long as they are living, their influence in preventing clotting will act upon the whole of the contained blood (Lister); and consequently thrombosis does not extend into them so long as there is sufficient blood-supply to keep them alive.

LATER CHANGES IN THROMBI.—These are:—decolorisation (when red), resolution, organisation, calcification, softening (simple and infective), and putrefaction.

Decolorisation.—The first change in a red thrombus is a breaking-down of the red corpuscles. Their stromata become unrecognisable,

and the hæmoglobin is set free and in great part absorbed, though some may remain as granular hæmatoidin. As a result, the thrombus loses its deep red colour and acquires a finely mottled reddish-grey tint. The process begins in the centre, and takes weeks or months before it is completed.

Resolution.—That many thrombi disappear is certain; for when it was the custom for venesection to be performed at regular intervals, the repeated bleedings were frequently effected from the same vein. In modern times also, re-establishment of the circulation is known to have occurred through spermatic veins and through the superficial veins in the leg, in cases where thrombosis had undoubtedly taken place. The steps of the process are not known. In some cases of death from septic poisoning, appearances found in vessels which have been tied indicate that thrombi, formed before the onset of the fatal disease, have broken down.

Organisation has been mainly studied in thrombi forming in ligatured vessels. The effect of the application of a ligature is usually to cut through the middle and internal coats of the vessel; the ends of the divided coats contract and retract somewhat, turning up and down into the lumen of the vessel; and the constricted external coat is all that is left in the grasp of the noose. In a few hours a red thrombus forms, conical in shape, and adherent by its base to the inverted inner and midde coats. For two or three days it extends, until it finally reaches the junction of the first collateral branch—often, for some unknown reason, stopping short of this on the distal side. Meanwhile, it has become firmer, drier, and more widely adherent about its base to the artery. The area of adhesion progresses, as the thrombosed piece of vessel contracts upon the clot, until it becomes universal. By the second day a buffy nodule may be seen in the base of the deep red thrombus, and this rapidly increases, so that in a week or two the colour of the clot has disappeared. After some weeks or months this decolorised plug is found to have been replaced by connective-tissue intimately united with the artery, which has the appearance of a firm fibrous cord. The microscope gives the following explanation of the process:—The red thrombus consists of red corpuscles, with a few white, in the meshes of a fibrin-coagulum. The buffy nodule which grows into the base of the clot is formed of small round cells, which at first are undoubtedly leucocytes migrated from the vasa vasorum injured by the ligature. But there is a difference of opinion as to the origin of those formed after (say) the third day. By this time

the cells of the part have recovered from the injury done them by the wound and ligature. It has been maintained that the new cells are all *leucocytes or their progeny.* Senftleben secured between double ligatures pieces of vessels, and put them into the abdomens of rabbits — an experiment which is practically repeated in the bits of vessels which lie *beyond* the ligature in all aseptic stumps. He found that they became filled with connective-tissue containing well-developed spindle-cells. It is, however, by no means certain that these spindle-cells were derived from leucocytes (p. 103); and even if they were, the ability of white corpuscles to form the new tissue would not exclude endothelium from also doing so, as a regenerative process. A more probable explanation is that the organising tissue arises from the endothelium or from the deeper layers of the intima. The intima is often found thickened and the internal elastic lamina simultaneously obscured or broken up. Processes can be traced from the lining membrane displacing the original clot. However formed, the cell-mass is penetrated by blood-vessels, which form as in granulation-tissue (p. 111). The cells become spindle-shaped or branched (Fig. 96), fibrillation appears either in them or in the ground-substance between them; many cells disappear as the fibres increase, the latter contract, and many vessels are obliterated, the result being—the fibrous cord above mentioned. This is called organisation of a thrombus; but it is evident that the original thrombus disappears entirely, and has nothing to do with the process which goes on in the round-celled mass, the origin of which we have discussed. The vessel-wall is converted into fibrous tissue, and blends with that of the clot.

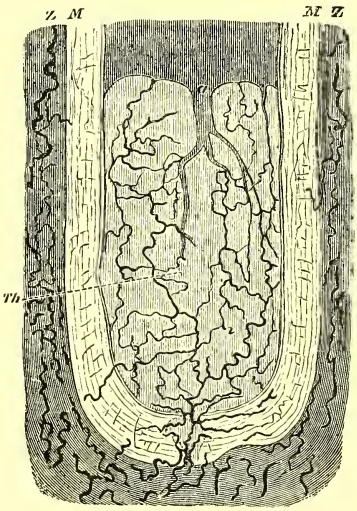


FIG. 96.—*Longitudinal Section of the Ligatured End of the Crural Artery of a Dog, fifty days after the application of the ligature.* Showing the newly-formed vessels in the thrombus and their communication with the vasa vasorum. *Th.* Thrombus. *M.* Muscular coat. *Z.* External coat and vasa vasorum. × 20. (O. Weber.)

In certain cases, channels are formed in the new tissue: these

communicate both above and below with the lumen of the vessel, and thus the circulation is more or less completely re-established. They are probably due to dilatation of the vessels of the thrombus (though why this should occur in some cases and not in others is unknown), and give rise to the *sinus-like degeneration* of Rokitansky. It is especially frequent at the junction of the common iliac veins in cases of "white leg," and leads to more or less perfect recovery. It is rare in arteries.

Organisation is most frequent in uniform, unstratified thrombi, and especially in those occurring in arteries. But long clots of this kind, such as occur after ligature of the lower part of the carotid, as well as large laminated thrombi, like those in aneurysms, may remain as more or less granular masses of non-irritant fibrin, without any sign of organisation.

Calcification.—This occurs in some clots, giving rise to phleboliths. These are especially common in the prostatic plexus.

Softening.—1. **Simple.** A thrombus which undergoes none of the previously described changes, often softens. This, in the majority of cases, is due to the chemical changes which the constituents of an aseptic thrombus undergo when no organisation occurs. They result in the formation of a more or less fluid, pappy substance, which has a reddish-grey colour, varying with that of the thrombus which is undergoing the change. To the naked eye the fluid often looks like pus, and the process is still spoken of as the *puriform softening* of a clot. But Virchow pointed out that the fluid consisted of the débris of corpuscles and fibrin—albuminous, fatty, and pigmentary granules. There may be a few recognisable white corpuscles in it, which have probably migrated from without. In cases of constriction of the mitral orifice of the heart, with consequent dilatation of the left auricle and slowing of the circulation, large clots undergoing this change may be found in the auricles. They consist of little more than bags of thick, grumous fluid. The outer laminæ generally form a firm case for the softened central part, and if the softening approach the surface, this case is often thickened at that point by the formation of fresh protective clot. Not infrequently, however, the encasing clot may be perforated and the contents discharged into the circulation. The larger particles may form emboli (p. 237), probably too minute to cause symptoms. When occurring in an artery or vein, circulation may be thus re-established through the thrombus. This process constitutes **canalisation** of a thrombus.

2. **Infective.**—But certain cases of **puriform** softening, similar, so

far as the naked eye can detect, to the above, are accompanied by all the symptoms of septic poisoning. Acute suppurative inflammation of the vein-wall is shown by the microscope; and any portions of the clot which enter the circulation are so intensely irritating as to cause suppuration wherever they lodge (see "Pyæmia and Septicæmia"). The difference between the two cases is that, in the latter form of softening, **micrococci** are constantly present, and it is to them that the infective properties of the broken-down clot are due. In the great majority of these cases the veins affected lead directly from a wound, and then the mode of entry of the specific micrococci is evident. In a small number of patients, also with wounds, the thrombosis and softening occur in veins having no kind of direct connection with the wound; here, too, the organisms have entered by the wound, and in some cases at least the thrombosis is secondary to a general septic infection. Finally, there remain a few instances in which no pathological breach of surface can be found for the admission of the germs; it is thought that, in these, they must have passed into the blood through the alimentary or respiratory mucous membranes.

Putrefaction.—This rare change is due to the entry into the clot of the putrefactive bacteria from some very foul, and often gangrenous, surface: the growth of these organisms converts the thrombus into a stinking yellow-red fluid, which is highly irritating.

RESULTS.—The results of thrombosis comprise certain changes in the walls of the vessels, more or less obstruction to the circulation, and embolism. These must be considered separately.

1. **Changes in the vessels.**—More or less alteration in the wall of the vessel is an invariable consequence of the formation of a thrombus. When the thrombus undergoes a process of *organisation*, it becomes, as already described, intimately united with the vascular wall. The latter in the first place becomes infiltrated with cells, and considerably thickened, but ultimately, together with the thrombus, gradually atrophies. It is when the thrombus undergoes a process of *infective puriform softening* that the most important changes, of an acute inflammatory nature, take place in the vessel. They are due to the irritation of the decomposing thrombus, and are most frequently observed in the veins, where infective thrombi are most liable to occur. The walls of such a vein are considerably thickened, so that to the *naked eye* it resembles an artery. The inner surface has lost its translucency, and is of a dead opaque colour. The adventitia and middle

coats are injected and present numerous hæmorrhagic points, which are often visible through the intima. The swelling of the wall is, under the microscope, seen to be due to dense infiltration with leucocytes, which conceals all normal structure (Fig. 97); while the innermost cells die, and are shed into the lumen of the vessel. Small

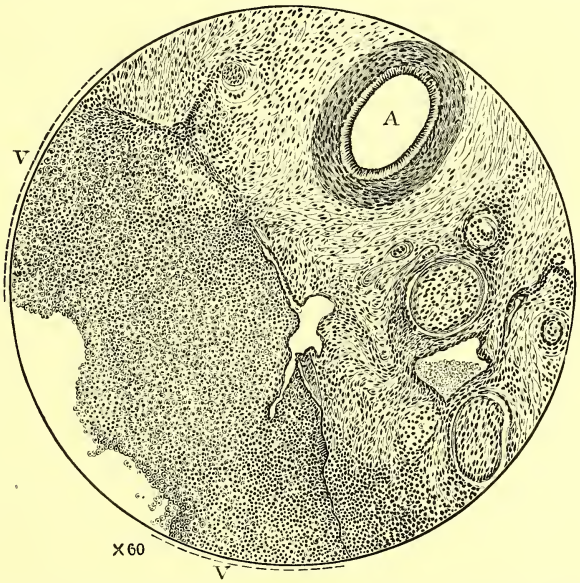


FIG. 97.—Section across a portal canal in a case of suppurative pylephlebitis arising in connection with "umbilical pyæmia." The vein-wall (V) is converted into granulation-tissue. Lumen of vein is below on the left. (Boyd.)

collections of pus may be seen in the external and middle coats. The neighbouring tissue may also become involved. These acute inflammatory changes in veins constitute what is known as **suppurative phlebitis**. Although most frequently due to thrombosis, they may also occur as the result of extension from adjacent suppurating tissues, in which case the thrombus, which also undergoes puriform softening, is *secondary* to the phlebitis. Similar changes are observed in the arteries. Septic arteritis, attacking a ligatured artery in a putrid wound, was formerly a most disastrous sequela to operations, being the commonest cause of secondary hæmorrhage, now so rarely seen.

2. **Obstruction to the circulation.**—The consequences of the obstruction to the circulation, resulting from the formation of a thrombus, will depend upon the rapidity and manner of its formation, the nature and size of the vessel obstructed, the situation and number of the collateral branches, and the force of the circulating current. The rapidity with which the obstruction is effected is of considerable importance, inasmuch as the more gradual the process, the longer is the time allowed for the establishment of a collateral circulation. For this reason the interference with the circulation caused by thrombosis is, for the most part, less marked than that which results from the more sudden obstruction caused by embolism.

In the veins, when thrombosis occurs in a vessel of small size and when collateral branches are numerous, as in the prostatic or uterine plexuses, the circulation is but little interfered with, and no symptoms of obstruction result. If, however, the main trunk of a large vein, as the ilio-femoral, becomes obliterated, the obstruction is followed by mechanical hyperæmia, the extent and duration of which will depend upon the facility with which the circulation can be restored by the collateral vessels. It must be remembered, however, that the valves in veins, when they exist, may, by preventing back-flow, offer a great impediment to collateral circulation. Thrombosis in the ilio-femoral vein frequently occurs, as already stated, in the later stages of many chronic debilitating diseases, especially in phthisis; also in the puerperal state, where it gives rise to the condition known as **phlegmasia dolens.** As the femoral is almost the only vein which carries blood back from the lower limb the effect of suddenly blocking it is marked. At first cyanotic, the *limb* becomes swollen, pallid, white, painful, and too tense to pit; and there is more or less tenderness along the *vein,* which feels enlarged, hard, and knotty. These symptoms vary greatly in amount; and to them are sometimes added those of lymphangitis and cellulitis. The extent of the *thrombus,* the number of collateral branches which it blocks, and the strength of the circulation, will do much to account for the amount of œdema; and it is probable that the more acute inflammatory symptoms are of septic origin. The circulation is, in most cases, ultimately restored; but if the impediment has been of long duration, the tissues become thickened, and the limb remains hard, indurated, and somewhat enlarged.

The results of obstruction in arteries will be considered at the end of this chapter. It is in tissues with "terminal" arteries that the

interference is most marked, and here hæmorrhagic infarction, which so often results from embolism, may occur, although, owing to the more gradual obstruction of the circulation, it is less likely to do so (see below).

3. **Embolism.**—Portions of the thrombus may be carried away by the circulation, thus constituting embolism. This, which is the most important result of thrombosis, will be considered in the following section.

EMBOLISM.

Embolism is the impaction of solid substances, circulating in the blood, in vessels which are too small to allow them to pass. The solid substances are termed **emboli**, and are of very varied nature.

By far the most frequent **sources** of emboli are **thrombi**, portions of which are carried from the seat of their formation by the circulation. Many **other substances**, however, may act as emboli. Among these are: (1) vegetations and calcareous or atheromatous masses separated from the valves of the heart, or from the inner surface of arteries; (2) portions of new-growths—as sarcomata—which, having perforated the vessels, have been carried away by the current; (3) parasites which have made their way into the interior of vessels; (4) fluid fat which has escaped from the fat-cells and entered open lymphatics, an occasional occurrence in fractures and contusions; and (5) pigment granules.

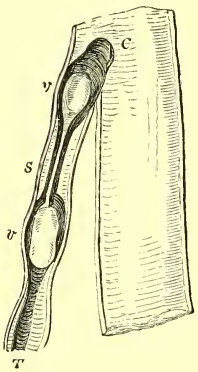


FIG. 98.—*A Thrombus in the Saphenous Vein.* Showing the projection of the conical end of the thrombus into the femoral vessel. *S.* Saphenous vein. *T.* Thrombus. *C.* Conical end projecting into femoral vein. At *v v*, opposite the valves, the thrombus is softened. (Virchow.)

A **thrombus** may produce emboli in various ways. (1) It may soften and break down, and its fragments be distributed by the blood-current. (2) Portions of a parietal thrombus, not filling the vessel, may be detached by the passing stream. But, on the whole, the most frequent way is (3) that illustrated by the accompanying diagram. A thrombus usually ceases at the junction of the vessel containing it with the first large collateral branch. The cardiac end of the clot, however, often extends as a firm conical projection into the lumen of this vessel (Fig. 98, *C*); and the strength of the blood-

current, which is the chief factor in preventing the further extension of the clot toward the heart, may break off this projecting end, and sweep it into the general circulation. Some sudden movement or exertion often determines, in these cases, the separation of the fragment which is to form the embolus. The veins are the commonest seat of thrombosis, and venous thrombi are common sources of embolism; the veins of the lower extremities and the jugular veins being the most frequent sites. Embolism from cardiac thrombi, whether attached to the walls or projecting from the valves, is also exceedingly common, and is produced in a similar manner; less frequently arterial thrombi give rise to the same result.

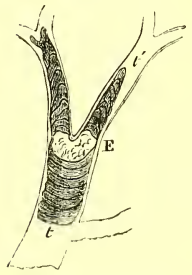


FIG. 99. — *Embolus impacted at the Bifurcation of a Branch of the Pulmonary Artery.* Showing the formation of thrombi behind and in front of it, and the extension of these as far as the entrance of the next collateral vessels. E. Embolus. *t t'*. Secondary thrombi. (Virchow.)

Emboli become arrested in the first vessels they reach which are too small to allow them to pass. Usually, therefore, the seat of impaction will be at the bifurcation of the vessel, or at some point where, from the giving off of large branches, the calibre diminishes suddenly (Fig. 99). The particles may be so small as to pass through even the finest capillaries, and not give rise to any symptoms; or they may pass through large capillaries, to be arrested in a finer set beyond; but as a rule they are impacted either in the first set of capillaries to which they come, or in some larger vessel between this set and their seat of origin. Thus, emboli originating in the systemic veins or in the right cardiac cavities, will most commonly become arrested in the vessels of the lungs. Emboli originating in the pulmonary veins, the left cardiac cavities, or the arteries, will be similarly impacted in the systemic arteries and capillaries, especially in those of the spleen, kidneys, and brain. Finally, emboli originating in the portal venous system will block branches of the portal vein in the liver. With the exception, therefore, of emboli originating in the portal system, the seat of arrest is the arteries or capillaries.

Emboli are carried usually in the direction of the main current; hence those carried by the aortic stream pass into the thoracic aorta more commonly than into the carotid or subclavian vessels, and into the left carotid or left renal artery more often than into the

corresponding artery of the opposite side. Gravitation also influences the direction in which they are carried, especially those of large size, which move somewhat more slowly than the blood-stream; hence, they are more common in the lower lobes and posterior parts of the lungs than in the superior and anterior portions of these organs (p. 251).

It is not uncommon to find that the small vessels of an area, of which the supplying artery is plugged, also contain emboli. This may be accounted for in *two* ways. *First*, if, as is frequently the case, the arrest takes place at a point of bifurcation, the embolus may partially fill both branches, allowing a small stream of blood to pass; this may break off portions of it, and so produce secondary emboli, which become impacted in the smaller divisions of the same main trunks. The *second* mode is by the detachment of several small emboli from some distant source, which subsequently yields a mass large enough to stick in the main trunk. It is found experimentally that small bodies injected at intervals into the jugular vein are sometimes swept into the same division of the pulmonary artery.

The amount of obstruction which immediately follows the arrest will depend upon the *nature* of the embolus as well as upon its size and shape. If the embolus be from a soft, recently formed thrombus, it will be at once moulded to the cavity of the vessel, which will thus be immediately and completely plugged. If, on the other hand, it is irregular in shape and firm in consistence, as when derived from a calcified cardiac vegetation, it may not completely fill the vessel, but allow a small current of blood to pass it.

The arrest of the embolus, and the consequent obstruction to the circulation, is followed by the formation of **secondary thrombi** behind and in front of it, which extend as far as the junction of the first large collateral vessels (Fig. 98). If the embolus does not completely fill the vessel, thrombosis leads to the deposit of successive layers upon its surface until the occlusion of the vessel is complete, and then the secondary thrombus extends, as in the former case, until it meets with a current of blood strong enough to arrest its progress. If the embolus is a portion of a soft thrombus, it will in most cases be impossible to distinguish it from the secondary thrombus which surrounds it. If, however, it is a calcareous mass, or a portion of an old thrombus, it may usually be distinguished from the more recent secondary coagulum.

Emboli may, in rare cases, become absorbed. They may also, when derived from thrombi, soften or become organised. The changes in

the secondary thrombi are similar to those already described as occurring in the primary (p. 230).

RESULTS.—The results of embolism are—(1) those depending upon obstruction to the circulation, and—(2) those produced by the irritation of the emboli.

From the facts disclosed in the preceding paragraphs it may now be inferred that embolism of either the pulmonary or the systemic veins is practically a mechanical impossibility; but that in any of the remaining vessels — arteries, capillaries, and portal vein — we may expect its occurrence. As embolism of the arteries is followed by very different results to that of the capillaries, the two conditions must be considered separately. For our present purpose the portal vein will be grouped with the arteries, from which it differs mainly in its lower blood-pressure.

Arterial Embolism.

1. **OBSTRUCTION TO THE CIRCULATION.**—The results to the circulation depend chiefly on the extent of the arterial anastomoses in the affected part.

Sudden and complete obstruction of some arteries—such as the radial or a second or third branch of the mesenteric—is practically without effect upon the circulation, which is carried on through the large vessels which anastomose with those branches of the obstructed artery which are given off below the seat of the obstruction. Yet ligature of the common carotid is occasionally followed by cerebral softening, easy though it would seem, when only one of the arteries supplying the circle of Willis is blocked, for the cerebral circulation to be efficiently maintained.

In other cases there is some, perhaps even very great, difficulty in effecting the re-establishment of the circulation. This is owing either to the small number and size of the vessels anastomosing with the branches of the obstructed vessel, or to some disease of these vessels interfering with their normal power of dilatation. On ligature of the femoral artery the limb becomes pale, and its surface-temperature falls many degrees. In this condition it remains several hours; then, if all goes well, the superficial vessels dilate, the circulation through them proceeds with undue rapidity, and the surface-temperature rises some degrees higher than that of its fellow. This reaction

gradually disappears, and ultimately the part may remain abnormally cool.

On the other hand, the part deprived of its blood-supply may die *en masse*. Between the two extremes of recovery and death, there are many possibilities—from death of a single toe upwards. The part which ultimately dies may remain pale and bloodless, and gradually mummify; but usually it becomes more or less swollen with blood, driven into it by a pressure insufficient to send the blood right on through the veins: fluid and cells pass into the tissues, organisms thrive, and invade the part, and moist gangrene results. Similarly, embolism of an ultimate branch of the mesenteric, with secondary thrombosis obstructing the vessels on either side, will lead to a partial necrosis of a small segment of bowel and hæmorrhage into its lumen (vide infra), probably ending in recovery; but embolism of the main trunk of the vessel causes gangrene of the whole intestine.

Infarction.—This seems the best place to discuss *infarction*—a process often produced by embolism, but not infrequently due to other causes. In some organs, such as the spleen and kidney, the arteries have capillary, but no arterial, anastomoses with the neighbouring vessels. Such arteries are called *end* or *terminal* arteries. Each of these arteries supplies a conical compartment of the organ in question. The base of the cone is on the surface of the organ, while its apex points towards the centre, and corresponds to the point of entrance and exit of the artery and vein respectively. The possible means of access which the blood has to such a portion of tissue are, (1) the main artery and vein just mentioned, (2) the small vessels passing from the capsule into the cortical part of the organ, and (3) the capillary anastomoses with the neighbouring vessels on each side.

If, by means of embolism or thrombosis, the main artery supplying one of these conical segments of tissue becomes blocked, necrosis and other degenerative changes will occur in it; for the capsular vessels and the lateral anastomoses together are unable to maintain the nutrition of the part. As seen post-mortem these cones or, as they are then called, infarcts, when cut from base to apex, have a very typical triangular section (Fig. 101). Two varieties are described: (1) the **white** or **anæmic** infarct, and (2) the **red** or **hæmorrhagic** infarct. A *white* infarct is pale-yellow, and has its base level with or depressed a little beneath the rest of the surface of the organ. A *red* infarct is blackish-red and has a slightly raised base. Recent infarcts of both kinds are surrounded by a hyperæmic zone. *Red* infarcts are common

in the lungs, spleen, and kidney, and are occasionally found in the intestine. *White* infarcts, when primary, are found in the brain, retina, and the muscular walls of the heart.

Microscopic examination of a *white* infarct will reveal coagulation-necrosis and fatty degeneration of its tissue-elements. Sometimes transudation from surrounding parts supplies sufficient nourishment to keep alive the connective-tissue stroma; the nuclei then stain with logwood (Fig. 101).

In the *red* infarct the tissue is so crammed with blood-corpuscles that the degenerative changes are often obscured.

Some *white* infarcts contain granules and crystals of altered blood-pigment. These are considered to be a later stage of *red* infarction in which the rest of the hæmorrhagic extravasation has disappeared.

It is very important to remember that all tissues do not equally resist the effects of anæmia—those of the skin and muscle are most resistant; those of the brain and intestine least. A piece of strangulated gut dies more rapidly than a tied-off ear. This power of resistance is not the same in all individuals.

Cessation of function soon follows cessation of nutrition. The effects of this may be extremely serious: thus, plugging of one of the larger cerebral arteries is generally followed by sudden loss of consciousness and paralysis; plugging of the pulmonary artery by sudden asphyxia; and plugging of one of the coronary arteries by sudden paralysis of the heart.

Pathology of Infarction.—Very different explanations have been offered of the exact manner in which infarcts are produced.

Arguing from the above data, Cohnheim offered the following explanation. In his opinion, the first effect of the plugging of a terminal artery is the stoppage of the blood passing through it; the arterioles contract and empty themselves; but being deprived of their blood-supply they subsequently dilate and the pressure in them is thus reduced to *nil.* Venous pressure, though low, is in excess of this, and so blood regurgitates from the veins to fill the capillaries and arterioles on the peripheral side of the plug—as may be seen with the microscope in the tongue of a frog, one of whose lingual arteries has been tied. The arteries round about the area dilate, and their capillaries become full of blood; but even with this assistance the blood-pressure in these circumferential capillaries is still insufficient to force the blood through more than a few of the outlying capillaries of the obstructed area. Consequently such an area will be dark from the presence of

stagnant venous blood, but surrounded by a ring of arterial redness. Later on, the escape of red corpuscles into the tissues will darken the mass still further. This occurs without any rupture of vessels, just as happens in venous congestion (p. 214). Finally, secondary thrombosis of the vein and other vessels is said to occur in the area (Fig. 100).

The changes which usually result from deprivation of arterial blood were studied experimentally by Cohnheim. If the ear of a rabbit be emptied of blood, ligatured at its root for eight to ten hours, and the blood be then allowed to circulate, the organ becomes exceedingly red, swollen, and œdematous. When examined microscopically the vessels are found to be dilated, and numerous *white* blood-corpuscles are seen to have escaped from them into the surrounding tissue. The longer the part is deprived of blood, the more abundant is the subsequent infiltration with leucocytes; and when the obstruction has lasted twenty-four hours small extravasations of *red* corpuscles also occur. If the ligature remain on for forty-eight hours the ear dies. Cohnheim concluded that when blood-vessels with their vasa vasorum are deprived of circulating blood for a sufficient length of time they lose their power of retaining the blood, and allow, first the liquor sanguinis and leucocytes, and subsequently red corpuscles, to escape from them, the escape taking place only through the capillaries and venules. The whole process can be watched in the tongue of a frog to the base of which a ligature has been applied. For the walls of blood-vessels to be thus altered, interference with the circulation must be very complete—a very little vascular supply serving to prevent the above phenomena. Still, it is a wide-reaching fact, which must always be borne in mind, that imperfect nutrition, however slight, is a step towards death, and must render tissues less resistant to injury. These observations explain all the changes, from œdema to moist gangrene, given above, which may follow ligature of the main artery of a limb.

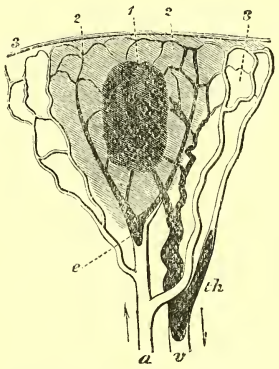


FIG. 100.—*Diagram of a Hæmorrhagic Infarct.* *a*. Artery obliterated by an embolus (*e*). *v*. Vein filled with a secondary thrombus (*th*). 1. Centre of infarct which is becoming disintegrated. 2. Area of extravasation. 3. Area of collateral hyperæmia.

(O. Weber.)

Cohnheim thought that when emboli blocked terminal arteries, the result was almost always hæmorrhagic infarction. In his opinion exceptions to this rule were due either to the veins of the part being valved or thrombosed so that regurgitation was prevented, or to the part being so placed that gravity strongly favoured the return of blood by the veins. In *these* cases the area remained pale and bloodless. He considered that some *apparent* exceptions were owing to the existence of fine arterial anastomoses with certain arteries, of which the great majority were *really terminal.* Thus anastomoses of the bronchial artery with the pulmonary might sometimes ward off infarction in the lung; and the presence of branches of the hepatic artery might similarly prevent infarction of the liver resulting from embolism of a branch of the portal vein. One reason, according to Cohnheim, why infarcts are so much commoner on the surface than in the substance of an organ is, that in the former situation the whole base is almost absolutely cut off from collateral supply.

Litten disputes the truth of Cohnheim's explanation of the whole process of infarction. He shows that the infarction of the kidney which follows ligature of the renal artery cannot be due to regurgitation from the renal vein, as it is most intense when the renal vein is itself simultaneously ligatured. Under these conditions the kidney swells, becoming first congested, and then infarcted. The congestion begins in the subcapsular zone of the cortex, and at the bases of the pyramids nearest the attachment of the pelvis. This congestion is due to the continued supply of the organ by small arteries (now much dilated) which spring from the lumbar, supra-renal, and phrenic, and pierce the capsule; as well as by others which spring from the spermatic, and run up along the ureter. If the renal vein is left open, the kidney swells more slowly, because some of the blood entering from these arteries can then escape by the vein; the venous stream is therefore away from, not towards, the kidney. But the completion of the proof that the infarction is due to supply through these arteries, and not to venous reflux, is afforded by an experiment which shows that, when these are detached, infarction does not occur. *One* kidney is shelled out of its bed of fat, and its artery is thus rendered really terminal. The renal arteries on *both* sides are then tied, while the veins on both sides are left patent. The "shelled" kidney now becomes slightly congested, but, as a rule, no venous regurgitation occurs; the organ remains lighter and smaller than its fellow, and does not become engorged with extravasated corpuscles. In the opposite

kidney typical infarction occurs. It would seem, therefore, that in many cases, when the main artery and its small collaterals are tied, the pressure in the renal vein is not sufficient to overcome the resistance in the capillaries and to distend them with venous blood, much less would it be able to do so when the capsular arteries are pumping blood into the cortex, and thus increasing the intracapsular pressure. If, by coughing or vomiting, the pressure in the renal vein is raised, infarction is more likely to occur; and it is produced in its severest

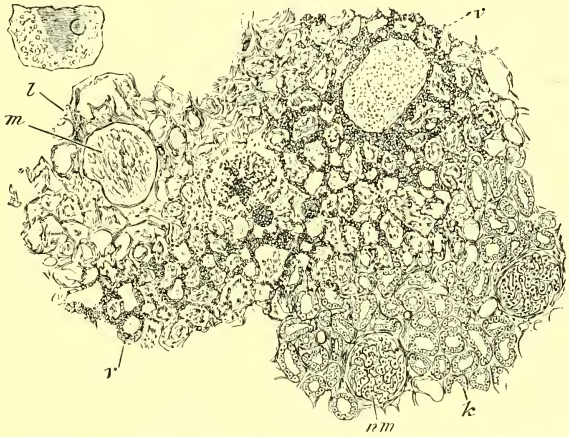


FIG. 101.—Above on the left is a representation (natural size) of a section through a recent infarct of the kidney: the circle marks roughly the part magnified and drawn in the main figure. *k* points to healthy kidney; *nm* of a normal Malpighian tuft; *v* to an area in which the vessels are crammed with red corpuscles, and the tissues are more or less degenerate; *l* and *m* to kidney substance and a Malpighian tuft which are too degenerate to stain. (Boyd.)

form by clamping the vena cava inferior above the entry of the renal vein. These observations were extended with similar results to the spleen and lung. Since then, anæmic infarcts in the spleen have been found associated with thrombosis of the splenic *veins* without any obstruction in the *artery*.

In the great majority of cases, when a truly "terminal" artery is blocked, no infarction occurs. The area formerly supplied by it remains pale and anæmic, and microscopic examination reveals no trace of red corpuscles. This is seen in cases of embolism of the cerebral arteries (white softening) and of the central artery of the retina.

When an artery of some part (*e.g.*, limb) in which the veins are valved becomes blocked, no reflux can occur, but infarction may. Such infarction is rare, because these parts generally have a rich arterial supply sufficient to carry on the circulation; it is most likely to follow blocking of the *main* artery (p. 241).

Litten agrees with Cohnheim that the red corpuscles escape by diapedesis, but considers that this is due to the distension of the capillaries and small veins by the mechanical congestion. It almost immediately follows the application of the ligature, before anæmia has had time to effect any marked change in the vessel-walls; and indeed, if a ligature be placed on the artery of a "shelled" kidney, and

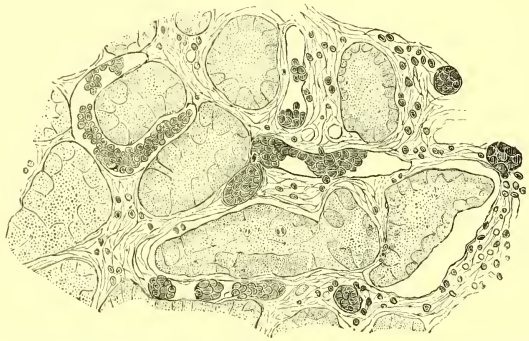


FIG. 102.—*Embolic Kidney.* From a case of aneurysm of the abdominal aorta: many small yellow-white patches were scattered through the cortices of the organs. Essential cells fattily metamorphosed, connective-tissue cells still capable of staining. × 200.

removed after four hours, no fresh blood enters and no escape of corpuscles occurs.

It would seem that the true reason why red infarcts are found so frequently on the surfaces of the organs in which they occur is not that the base is almost entirely cut off from its blood-supply, but that there the small capsular arteries enter, and that through these blood is still driven into the area.

Litten's experiments are conclusive so far as the kidney is concerned. Cohnheim's *regurgitation theory* probably holds good for a few cases, and in its favour it must be remembered that, in the majority of cases in which simple embolisms from cardiac valves occur, there is "back-telling" (p. 17) upon the lungs, and venous pressure is abnormally high. Nor should it be forgotten that the resistance offered to regur-

gitation from the veins by the capillaries of the tongue or ear is probably much less than that offered by those of the firm kidney within its elastic capsule.

IRRITANT EFFECTS OF AN EMBOLUS.—A **simple embolus**, such as a bit of non-infected fibrin or a fragment of a calcareous plate, causes slight irritation of the vessel where it lodges. Such an embolus, with its secondary thrombi, will usually be absorbed or become organised. This irritation may occasionally cause so much inflammatory softening of the vessel-wall that it yields before the blood-pressure, and an aneurysm results (see "Arteries"). This is now held to be the pathology of most aneurysms occurring in people too young to be suffering from atheroma or acquired syphilis; and, as the emboli are usually small or of moderate size, dilatations from embolism affect especially the cerebral arteries and the smaller arteries of the limbs—from the size of the brachial downwards.

An **infective embolus** is one which has brought with it from its source organisms capable of growing within the body—at all events, in the dead or greatly depressed tissues of an infarct—and which thus gives rise to bacterial changes at the point where it is arrested. The result depends upon the intensity of the irritation which the particular bacteria can excite: in cases of rheumatism they often seem to render the embolus but little more irritant than simple fibrin; but in pyæmia the micrococci cause secondary suppuration (see "Pyæmia").

LATER CHANGES IN EMBOLISM.—These depend upon the two considerations just discussed: (1) the extent to which the circulation is interfered with, and (2) the amount of irritation caused by the embolus.

1. **Small infarcts.**—In the case of *small red infarcts,* if the embolus is free from organisms, the coagulated blood gradually loses colour, becoming brown or yellow, and absorption proceeds slowly. In the case of *small anæmic infarcts,* the tissue-changes are more clearly seen than in the red infarcts, where they are obscured by the extravasated blood. In these white infarcts, lymph reaches the part by transudation from parts around, the cells swell, loose their nuclei, and blend—in fact, undergo coagulation-necrosis (p. 22), and thus form the well-known white wedges. The more external portions of this mass of coagulated blood and necrosed tissue become infiltrated with leucocytes. In this area fibrous tissue subsequently develops; this

contracts, and ultimately a depressed scar may be all that remains to indicate the change. For some time, whilst these secondary changes are taking place in the infarct, its most external portions are surrounded by a red zone of hyperæmic tissue. This is exceedingly characteristic.

2. **Large infarcts.**—In the case of a *large infarct,* the central portions may disintegrate and soften. This may subsequently dry up and leave a depressed scar.

3. **Infective softening.**—If an embolus is derived from a part where an infective inflammation is going on, it sets up a similar inflammatory process, both in the vessel, within which it becomes impacted, and also in the surrounding tissues. These septic inflammatory changes lead to the formation of abscesses, which are known as **embolic** or **metastatic abscesses**. Microscopic organisms are almost invariably found in these abscesses, and it is to them that the infective properties of the embolus are probably due. No more suitable nidus for their development can well be imagined than a tissue in which infarction and necrosis have occurred, and which is kept moist at the temperature of the body. Infarction is not an essential antecedent of a metastatic abscess. If the metabolism of the tissue in which the embolus lodges does not destroy the organisms, but affords them suitable pabulum, inflammation will ensue. This subject will be considered further in the chapter on "Septicæmia and Pyæmia."

4. The **other** possible **results** of embolism have been referred to on p. 241.

Capillary Emboli.

These generally consist of fat, masses of organisms, clumps of white blood-corpuscles, pigment-granules, or air. In fractures, contusions of subcutaneous tissue, ruptures of fatty liver, acute osteo-myelitis, and other morbid conditions in which fat-cells are broken up and the fat set free, the droplets are absorbed by the lymphatics and veins, especially when pressure in the part is increased by inflammatory effusion or hæmorrhage. On reaching the right side of the heart, they are carried into the pulmonary arterioles and capillaries, where their presence may easily be demonstrated by staining with osmic acid (Fig. 103). One by one these soft and easily moulded plugs are swept on to the left side of the heart, and distributed by the systemic circulation to other organs, in which also they may be very numerous.

For a time, fresh emboli are constantly reaching the lungs; but when this ceases the fat-masses are passed on to other organs and eliminated, in part at least, through the kidneys. This fat-embolism is believed by some to be the cause of death after simple fractures—a very rare event. But, as large quantities of fat may exist in the lungs and other organs of animals without causing any symptoms whatever, some scepticism is justifiable. If a sufficiently large number of the capillaries of the lung, or any other organ, be blocked by fat, its function will, of course, be interfered with; and in the case of some organs this would mean speedy death. It is probable that the lungs always contain,

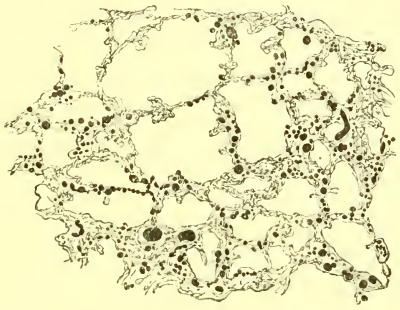


FIG. 103.—*Fat-Embolism of Lung.* From bad compound fracture of leg and severe subcutaneous laceration. The black masses are drops of fat, stained with osmic acid, lying in capillaries and arterioles of alveolar walls. × 40. (Boyd.)

proportionately, many more emboli than any organ supplied by the systemic circulation. It has been ascertained that half the pulmonary blood-path may be obstructed without disturbing the circulation at large (Cohnheim). We must therefore suppose that, as a rule, the passage of fat on to the systemic circulation keeps the number of plugged capillaries below the point of danger. In acute osteo-myelitis it is probable that the fat-drops may serve as carriers of pyogenic cocci from the seat of inflammation, and cause their impaction in vessels which they would otherwise pass through freely.

Clumps of leucocytes form emboli, and therefore petechiæ, in septic fevers (Hüter). Air entering the veins, may give rise to embolism. Here, as in fat-embolism, the air-plugs have little effect: to cause death, air must be injected so quickly and in such quantity that the blood in the right heart is churned into foam, upon which the viscus

fruitlessly contracts. Pigment-granules, probably parasitic in origin, have caused capillary embolism in malaria (see "Malaria").

Thrombosis and Embolism of the Brain.

Thrombosis and embolism are the most common causes of **cerebral softenings.**

Softening from Thrombosis.—This is commonly the result of atheromatous, calcareous, or syphilitic changes in the **cerebral arteries.** Such changes favour the occurrence of thrombosis, causing diminution in the lumen of the vessels, roughening of their internal surface, and impairment of their elasticity and contractility. As a result of the interference with the supply of blood, the cerebral substance undergoes a more or less rapid process of necrosis (p. 60).

Thrombosis may also occur in the **cerebral sinuses and veins.** Thrombosis of a sinus may be **primary,** and fall under the heading of marasmic (p. 227), or it may be **secondary** either to (1) disease of some adjacent part, such as of the bone in inflammation of the middle ear; or (2) to extension of a thrombus along a vein—as in the case of the orbit—from an inflamed part to the sinus into which it opens. The result is great distension of all veins opening into the sinus, œdema of the area whence they draw their blood, minute hæmorrhages, especially in the vascular cortex, and softening from impaired nutrition.

Softening from Embolism.—The softening resulting from embolism is, for the most part, entirely dependent upon the obstruction to the circulation caused by the embolus and by the resulting thrombosis. It is rapidly induced, and is often attended by the extravasation of blood in its neighbourhood, when it constitutes one form of acute red softening (p. 62). If the interference with the circulation be slight, and there be no extravasation of blood, the softened portions are white in colour (p. 60). The vessel most frequently blocked is the middle cerebral artery; and in the majority of cases it is that of the left side. In almost all cases in which softening of the cerebral substance results from embolism, it is due to arrest of the embolus in one of the vessels *beyond* the circle of Willis, because here the circulation cannot be readily restored by the collateral vessels. Softening, however, does not necessarily follow the blocking of a cortical artery, for communication between these branches is freer than is often supposed.

Engorgement of the area beyond an obstruction in a cerebral artery is an exceptional occurrence, but it is sometimes so marked as to cause rupture of a large artery beyond the obstruction, and fatal hæmorrhage some days after the embolism. For reasons just stated, this is a far more likely occurrence in obstruction of cortical than of larger or basic vessels. When interference with the circulation is attended by vascular engorgement and extravasation of blood, the softened portion, in the early stage, is either of a uniform dark-red colour or presents numerous hæmorrhagic points. The softening is most marked in the centre, whilst the hyperæmia and redness may extend for some distance around it (p. 62). The surrounding capillaries are dilated and filled with coagula, and granular corpuscles envelop their walls. In a more advanced stage all trace of nervous structure is lost: the softened mass becomes decolorised, and passes from a dark-red colour to a chocolate, brown, yellow, or even white. It may liquefy and form a cyst with clear contents and a fibrous wall. More commonly, however, it is gradually absorbed, being replaced by fibrous tissue, which contracts; and ultimately a cicatrix, with hæmatoidin crystals, may be all that remains.

Infarction of the Lung.—Pulmonary Apoplexy.

This condition is sufficiently distinctive to merit separate consideration. The so-called infarcts of the lung are most commonly met with in cases of mitral stenosis, and to a less extent in those of mitral regurgitation. They are found in the lower lobes, and in the lower and outer parts of the upper lobes. In most cases they are irregularly conical, but occasionally nearly globular. In diameter they vary from a fraction of an inch to that of an entire lobe. Blackish-red, firm, with well-defined margin, often multiple and occasionally confluent, they present superficial resemblances to tumours on the one hand and to lobar pneumonia on the other. From the former they are distinguished by their colour, shape, position, and the conditions under which they occur; from the latter, by their number, shape, darker colour, and better defined limits. They are not infrequently the starting-points of a hypostatic pneumonia, and are then less easily recognised. In such cases the adjacent portion of the visceral pleura is roughened by the inflammatory exudation on its surface; while by the same factor in the substance of the organ the masses are welded, the colour mottled, and the edges obscured.

Mode of formation.—There can be no doubt but that these masses consist mainly of extravasated blood; but there is considerable difference of opinion concerning the reason of its appearance in the tissues. They are regarded as the several products of **embolism, thrombosis,** or **rupture** of the pulmonary vessels.

In favour of **embolism** of one or more branches of the pulmonary artery, may be urged (1) the frequent existence of a thrombus in the right auricle; (2) the discovery of an embolus in the largest artery entering the infarct; and (3) the general resemblance which these masses bear to infarcts of the spleen and kidney. *Against* **embolism** as the sole cause, are (1) the not infrequent absence, in these cases, of thrombosis and all other known causes of embolism either in the systemic veins or in the right auricle; (2) the still more frequent failure to find an embolus in any branch of the pulmonary artery itself; and (3) the complementary facts that embolism may be found without infarcts, and that artificial embolism in animals fails to produce infarction.

That **thrombosis** is, at least, an occasional cause of "pulmonary apoplexy" is inferred from (1) the existence, in a few of the cases, of atheroma in the pulmonary artery; (2) the presence of a thrombus (without any sign of embolism) in the main artery supplying the infarct; and (3) the extreme retardation of the blood-current at the time the "infarct" is formed. On the other hand, all these phenomena may exist without any infarction.

Unquestionably the most constant condition present in these cases is a long-continued and marked increase in the pressure in the pulmonary veins and capillaries. The numerous anastomoses of the bronchial vessels with the pulmonary veins, and the weak action of the heart which usually co-exists, co-operate with the increased pressure in distending the vessels and in lowering the nutrition of the vessel-walls, and thereby increasing their liability to **rupture**; while the enormous strain thrown upon the parts in coughing supplies an exciting cause. The chief objection to this explanation lies in the fact that all these conditions so frequently obtain without any infarction occurring (p. 38).

Grawitz has formed the opinion that all these "infarcts" are due to the rupture of newly-formed vessels. A careful examination of some fifty cases showed that the structure of the affected parts is in all cases similar. In the parts supplied by the bronchial vessels—*i.e.*, the sub-pleural, peribronchial, and interlobular tissue—Grawitz found

numerous large, tortuous, and, in his opinion, newly-formed arteries. In the neighbourhood of these he thought he could trace commencing hæmorrhages. But the most important of his results seems to have been his success in *producing* infarctions. This he accomplished by simultaneously compressing the bronchus and the pulmonary artery. The infarctions took some weeks to develop. He explains those cases in which emboli and infarctions have been found associated, by the suggestion that small peribronchial hæmatomata may so invade and damage the walls of the adjacent arteries as to give rise to the gradual formation of a thrombus which he thinks has often been mistaken for an embolus.

CHAPTER XIX.

FEVER.

By the term "fever" is meant an abnormal rise in the temperature of the body, together with other changes due to increased combustion of the tissues.

TEMPERATURE IN HEALTH.—It is usually stated that the normal temperature of the body is 98·4° F. It must, however, be remembered that the temperature not only varies in different parts of the body, but also varies slightly with the time of day, the age of the patient, and the surrounding temperature. The normal temperature of the *surface* of the body is always lower than that of the *internal parts*. Moreover, it is lower in proportion as we pass from the trunk towards the periphery, as well as more liable to variation from change in external conditions. To ascertain the temperature of the body for clinical purposes a thermometer is placed between folds of skin in the *axilla* (or, in the case of children, the groin), under the *tongue*, or in the *rectum*. If results are to be compared, it is essential that all observations be made in the same place, for the temperature in the axilla is generally half a degree lower than that in the mouth, and that in the mouth half a degree lower than that in the rectum. Again, the time of the observation must be stated, for the temperature rises during the day, reaches it maximum between five and eight P.M., and falls during the night to its minimum between two and six A.M.

Further, the average temperature of an infant or young child is slightly *higher* than that of an adult; and in the aged it may be slightly *below* the average in the adult. The full range between all these extremes is between one and two degrees.

The regulating (thermotaxic) mechanism is less easily disturbed as age advances. The temperature of young children is easily raised or depressed: an attack of crying may cause a distinct rise. In old age, on the other hand, when oxidative processes are feeble, the temperature is more easily depressed than raised. For this reason slight rises of temperature in the aged are of much graver significance than in the average adult, and in the former even acute forms of inflammation may be present without any accompanying rise of temperature. The effect of food is to excite metabolism in the large mass of gland-tissue connected with the alimentary tract, and to cause a slight rise of temperature: the taking of food may therefore quicken a rise or retard a fall. The effect of ordinary exercise is slight, but tends to produce a rise: severe exercise, such as prolonged running, may cause a rise of one or two degrees or even more. Mental exertion tends in a similar direction, and it is evident that the activity of all protoplasm must do so. The greater activity of the tissues and the combustion of the ingesta are the most obvious reasons for the higher temperature during the day. The diurnal variation is, however, said to occur in persons confined to bed and deprived of food, so that the explanation may lie in the diminution of tissue-activities during sleep. It is said that in those people who are in active work during the night, and are asleep during the day, the normal course of the temperature is reversed.

SYMPTOMS OF FEVER.—Since the introduction of the clinical thermometer the term "fever" has come to be almost synonymous with that of rise of temperature. This latter condition is certainly the most easily ascertained, the most readily recorded, and, on the whole, the most reliable symptom of fever. The course of the temperature in all febrile attacks is divisible into three stages: (1) the *onset,* or period of rise; (2) the *acme,* fastigium, or stationary period, during which the temperature is more or less at its height; and (3) the *fall,* decline, or period of defervescence.

The **onset** may be *sudden,* the temperature rising three to seven degrees before the end of the second day; or it may be *gradual,* rising every evening, and falling slightly every morning, until the full height is reached, as is seen in typhoid fever. The sudden onset is frequently

accompanied by an intense sensation of cold and a violent attack of shivering, known as a *rigor*. The temperature is at the time high, the vessels of the skin are contracted, and excessive loss of heat is thus prevented. In children in whom the controlling power of the nervous system is less developed than in later life, a *convulsion* often replaces the rigor. The gradual onset may be marked by slight chilliness, but very rarely by rigors.

The **fastigium**, or second stage, may be over in a few hours, or may last for weeks. The temperature may remain at a fairly constant level, or it may oscillate several degrees each day.

The **final stage** of fever, like the onset, may be sudden or gradual. When sudden, it is said to end by **crisis**. The drop is often accompanied by "critical" sweating, or diarrhœa. Sometimes the fall is so rapid and so marked that the patient may be in danger of dying, and may even die, of collapse. When the fall is gradual it is said to end by **lysis.** This is analogous to the corresponding form of onset, as the temperature falls by a series of morning drops, broken by slight rises in the evening. The special types of fever characteristic of some diseases are in all probability dependent on peculiarities connected with the growth of special parasites (see "Malaria"). When fever ends in death, the temperature generally rises just before this occurs, and may occasionally go on rising for a short time afterwards.

Febrile temperatures almost always exhibit a tendency to rhythmic daily **variation** like the normal temperature—being higher in the evening than in the morning. Sometimes the opposite is the case, and the temperature is then said to be of the *inverted* type. When the daily variation does not amount to much more than two degrees, the fever is termed *continued.* When the variation is greater than this, the fever is *remittent;* of this type *hectic fever,* which accompanies chronic suppuration, is a good example. When the drop between two maximum points reaches or falls below normal—so that there is a fever-free period—the fever is said to be *intermittent;* of this variety malaria is the type.

The **extent** of the rise of temperature varies greatly. Certain terms are sometimes employed to express the average height of the temperature. It is, however, quite as easy, and always better, to give the figures themselves. Above 107° F. the fever is called *hyperpyrexia,* and a temperature at or above this point, enduring for any length of time, is usually fraught with the greatest danger to life. When the temperature of the body as a whole reaches 109° to 110° F.

prompt measures are necessary to prevent death. As in sunstroke, this termination is possibly due to some decomposition of the tissues. So called *paradoxical* temperatures even up to 128° F. have been recorded as occurring in hysterical individuals, and in a few of them the most careful watching has failed *to detect* deceit. In some cases very high temperatures have recurred again and again. They are often quite local, the temperature on the opposite side being, for example, practically normal. They are accompanied by few or no symptoms. Wasting especially is absent. Hale White regards these cases as of central origin, due to perverted action of supposed calorific centres, comparable to the derangement of the motor centres in hysterical hemiplegia. Hysterical persons are very liable to disturbances of body-temperature.

High temperatures are generally accompanied by cloudy swelling of the tissues, and, if prolonged, by fatty degeneration: poisons circulating in the blood have very likely a share in producing this result (p. 63).

Apart from rigors and chilliness which are usually associated with the onset, the earliest symptoms, as regards the **nervous system**, are headache, incapacity for self-application, general sluggishness of mind, loss of self-control, and hyperæsthesia of the special senses. Then comes delirium—at first at night, and for short periods only, but later on often becoming more marked and even constant. Vague muscular pains are common in early stages: even in their absence, unwillingness for exertion is marked. The muscles waste rapidly and their movements become weak and tremulous. The nervous system has a large share in producing tremor and prostration, and is responsible for such a symptom as constant picking at the bedclothes (carphology). In fever the frequency of the **heart-beats** is increased. This result can be obtained experimentally by the application of heat. Yet the rapidity of the pulse bears no reliable proportion to the height of the temperature. It is much greater in some diseases than in others, for example, in scarlatina than in typhoid. The heart among other muscles fails progressively in quality and power, and, as it does so, its beat becomes more frequent and less effective. Here again the nervous system may be partly at fault—the inhibitory influence of the vagus being impaired. Similarly, arterial tone is progressively lost. The result of the progressive failure of the heart-force and arterial tone is that the pulse, which in a healthy individual at the commencement of a long fever is quick, full, strong, and often inclined to hardness

from high arterial tension, becomes, as the disease progresses, quicker, softer, and fuller, though no further rise of temperature has occurred. The softness and fulness of the pulse are due to loss of arterial tone while the heart-beat is still strong; the softness increases as the arterial tone yields. Later on, the size diminishes as the still more rapidly beating heart fails to fill the vessels. Ultimately, the pulse is very small, soft, and frequent, or as it is termed, *thready*. Increasing frequency of pulse with a steady or falling temperature is often regarded as *the* sign of a failing heart; though the "quality" of the first sound really affords an earlier indication of its approach.

Respiration is quickened. This change, like the increased frequency of the pulse, is possibly in some measure due to the effect of the rapidly heated blood—in this case, on the respiratory centre, as it can be induced experimentally by similar means. The oxygen absorbed and the carbon dioxide exhaled are both increased, sometimes in exact proportion to the rise in temperature.

Digestion is impaired, for secretions from the glands discharging into the alimentary tract are diminished. Appetite is lost (anorexia), and its place is taken by thirst. The tongue is dry and often furred. There is usually constipation, due probably to sluggishness of the intestinal muscle, to lack of secretion, and perhaps to absence of some of the normal stimuli to contraction. **Excretion**, as tested by the rapidity with which certain ingesta appear in the urine, is said to be slow in fever. Although the amount of fluid taken is larger than in health, the urine is small in quantity, has a high specific gravity, yields a copious precipitate of urates, and contains an excess of urea, uric acid, potassium salts, and pigment (pathological urobilin). The chlorides are diminished. With the excess of colouring matter in the urine, may be taken the fact that in fever there is a progressive *decrease* of red corpuscles and, according to some, corresponding *increase* in the amount of iron eliminated in the urine. According to Hayem both *hæmatoblasts* and *red corpuscles* are less numerous during the stationary period of fever. Directly the fall in temperature begins, the number of hæmatoblasts increases, reaching its maximum a day or two after the disappearance of the fever. During the following week it gradually sinks to normal. An increase in the number of red corpuscles and a simultaneous diminution in the *proportion of hæmoglobin* they contain, closely follow the increase in the hæmatoblasts. The rise in the percentage of hæmoglobin completes the return of the blood to its normal state.

The excess of *urea* is one of the earliest changes, and may even precede the rise of temperature. The excess is generally absolute. Sometimes it is only relative; that is, more is passed than would be excreted by a healthy man confined to bed on a similar diet. There is usually a marked increase at the commencement of defervescence: this is most likely due to an accumulation of its precursors in the blood or tissues.

POST-MORTEM RISE OF TEMPERATURE.—A slight rise of temperature often occurs after death, especially in those dying suddenly or of acute diseases. It is most marked in cases of fever due to the presence of a ferment in the blood, or in cases where death occurs with a high and rising temperature. Tetanus is probably the best example. The explanation is, that cessation of the action of the heart is not accompanied by immediate extinction of tissue-change. Thermogenic processes continue for a longer or shorter time; and thus, while the production of heat ceases gradually, the loss of heat, being largely dependent on the respiration and circulation, is cut down so suddenly, that the rectal temperature rises for a brief interval, and then falls as usual.

PATHOLOGY OF FEVER.—The foregoing account has shown that the essential condition in fever is increased thermogenesis due to increased breaking-down of the tissues and especially of the muscles; for the functions of the glands, the second great heat-producing organs, are almost in abeyance. As we have already indicated, by increased thermogenesis we mean that a febrile patient will produce more heat in a given time than a healthy person upon the same diet and under similar circumstances; not necessarily more than a healthy person on ordinary diet, though even this may be the case. While the febrile patient takes less food he absorbs more oxygen, and the increase in heat he produces is due to the excessive combustion of his tissues. Traube held that diminished loss of heat took the greater share in the maintenance of the raised temperature in the body of a febrile patient; and that this was brought about by an energetic contraction of the vessels of the skin. But such a contraction of vessels is by no means constant, and, when it occurs, is not of long persistence. Moreover, a high temperature and a freely sweating skin often occur together, and calorimetric observations have actually demonstrated the increased thermogenesis. If support is required

for the view that fever is dependent on increased destruction of tissue, it is found in the proportionately increased discharge of urea and carbon dioxide.

Some physiologists believe that **thermogenesis** is under the control of a cerebral centre or centres which control other thermal centres in the cord; but in the present state of knowledge it is impossible to speak certainly of the position of these centres, of their function (excitor or inhibitory), or of the paths of their afferent and efferent fibres. The effect of curarising an animal* would seem to demonstrate that, normally, heat-production in muscle—like contraction—takes place only in response to a stimulus along a thermal (catabolic) nerve; but it does not prove the impossibility of *directly* stimulating the muscle to produce heat, especially as we know it can contract after its motor nerve is dead. It is evident, therefore, that the causes of fever may induce the increased thermogenesis, either by acting *directly* upon the tissues or by acting on them *indirectly through the nervous system.* In certain cases—*e.g.*, nervous or hysterical fever, it seems impossible that the cause can act upon the tissues otherwise than through the nervous system; but, in the majority of cases, it may act either way, and until recently it has generally been assumed that the action has been direct from the blood upon the tissues.

Still, as we have already shown, thermogenesis may be increased enormously in health without any rise of temperature, and we must therefore consider that fever also involves a disturbance of the heat-regulating mechanism, or **thermotaxis**, whereby it fails *to maintain* the balance between heat-production and heat-loss. If this balance were maintained, as in health, we should have a stable temperature at a higher level than the normal. But the chief characteristic of the temperature in fever is its variability. Cold, food, excitement, effort, antipyretic drugs, all affect the temperature in fever much more markedly than the temperature in health. As MacAlister says, the

* MacAlister showed that the work-performing and heat-producing functions of muscle are to a certain extent distinct. Stimulation of a muscular nerve caused dilatation of its vessels, temporary contraction of the muscle, and increased production of heat. Fatigue and cold both interfered with the thermogenic function long before they impaired the power of contraction. On the other hand, poisoning by curare—which acts on the nerve-endings in muscle — paralysed the motor and thermogenic functions of the muscles simultaneously. If an animal, capable of maintaining a fairly uniform temperature (*homoiothermic*), be poisoned with curare, it becomes incapable of maintaining its temperature, which accordingly varies with that of the surrounding medium (*poikilothermic*), although the circulation of the blood is unimpaired and the normal rate of respiration is kept up.—*Lancet*, vol. i. 1887.

tolerably regular daily fluctuation of the temperature in fever shows merely that *all* the thermal processes are not utterly disturbed—some which are rhythmic in health remaining so in disease.

Like inflammations, fevers may be divided into the **infective** and **non-infective.** The **infective fevers** are those due to the multiplication in the body of a micro-parasite. This explanation serves for the group of "acute specific fevers," malaria and febrile diseases in which there is no inflammation present, at least in the early part of their course. These constituted the old groups of **primary** or **essential** fevers. In some (typhus, malaria) there is no inflammation; but in many, an inflammation appears (of throat, nose and eyes, skin, intestine)—too late and often too slight to account for the fever present. There are also the cases of fever **secondary** to a wound through which organisms have gained access to the body—*e.g.*, septic infection, pyæmia, erysipelas, and lymphangitis; and the large group of fevers secondary to inflammations (**inflammatory** fevers), practically all of which are infective. In most of these "secondary" fevers, the pyrogenous materials are manufactured by organisms in some definite part of *the body,* and are thence cast into the blood.

In the **non-infective group** we find first of all two wound diseases: (1) simple traumatic fever, and (2) its more intense form, acute septic poisoning or sapræmia (see "Septicæmia"). **Simple traumatic fever** ensues upon "simple" injuries (contusions and fractures). It is generally slight, and is most probably due to the absorption of fibrin-ferment (and very likely other pyrogenous bodies) from the seat of injury: possibly irritation of nerves—by the original injury or by fragments of bone or tissue—may have some effect in causing the fever, though *strong* irritation of a sensory nerve causes depression of temperature. **Aseptic traumatic fever** which occurs in aseptic wounds is probably due to the same causes as the simple traumatic. **Nervous (hysterical) fever** is supposed to be due to the influence of higher over lower thermal centres. The rises of temperature which occur in children, puerperal women and other weakly adults from various emotions, and other slight causes—*e.g.*, the rise which is so commonly found after an entertainment has been held in a hospital-ward—seem to be examples of nervous fever.

Further, cases of nervous injury or disease not uncommonly occur, in which one cannot help suspecting either that thermo-inhibitory centres or fibres are destroyed, or that thermogenic centres or fibres are irritated. Hale White has brought a number of such cases

together. In a most interesting case of bullet-wound of the head accompanied by fever, not otherwise explained, it was found that the motor area of the cortex, corresponding to Eulenburg and Landois' heat-centre in the dog, had been destroyed. The inhibitory influence of this centre may apparently be cut off, or destroyed by sudden and extensive intra-cranial hæmorrhage, or by hæmorrhages, scleroses and tumours of the brain so placed as to destroy inhibitory fibres or to irritate thermogenic tracts. It has long been known that injuries and tumours of the cervical cord, along which most thermal fibres must pass, are apt to cause marked fever. In a girl, with a fracture of the cervical spine, Teale recorded a temperature of 120° F., recovery ultimately occurring: some regard this as an instance of hysterical fever.

Lastly, there are many fevers of whose pathology we are still ignorant—*e.g.*, the fever met with in various anæmic states, in lymphadenoma, and occasional cases of malignant disease.

CHAPTER XX.

INFLAMMATION.

Inflammation may be defined as "the succession of changes which takes place in a living tissue as the result of some kind of injury, provided that this injury be insufficient immediately to destroy its vitality" (Sanderson).

HISTOLOGY.—The exact nature of these changes was, for the most part, ascertained by the experimental researches of Cohnheim. The method of investigation consisted in the artificial production of inflammation in transparent parts of the lower animals, and in the observation of the process thus induced. The parts employed have been the foot, tongue, and mesentery of the frog; the tongue of the toad (the best for many purposes); the mesentery of the rabbit; and the wing of the bat. The similarity of the different observations has shown that the process is essentially the same in warm and cold-blooded animals; and by microscopic examination of the lip by reflected light, Hüter proved that it is the same in man. The

Process of Inflammation is generally described under three headings :—

1. *Changes in the blood-vessels and circulation.*
2. *Exudation of fluid and of blood-corpuscles from the vessels.*
3. *Changes in the inflamed tissues.*

Though separated for purposes of description, it must not be supposed that these changes occur successively in the order in which they are placed ; on the contrary, *they all go on together.*

1. **Changes in the blood-vessels and circulation.**—Changes in both blood-vessels and circulation are *absolutely essential* to the existence of inflammation. This is true of non-vascular as well as of vascular tissues. In the former, which comprise the cornea and cartilage, the changes occur in the adjacent vessels from which these tissues derive their nutritive supply. The nature of the changes may be studied in the mesentery of a curarised frog. Briefly, they are as follows :—

The first effect of injury of the mesentery—mere exposure to the air being sufficient for the purpose—is to cause **dilatation** * of the *arteries,* which gradually extends to the veins and capillaries. The dilatation of the arteries commences at once, and is not preceded by any contraction. It increases, steadily and slowly, for about twelve hours, and is accompanied by an increase in the *length* of the vessels, so that they become more or less tortuous. It affects the arteries chiefly, then the veins, and slightly the capillaries. This enlargement of the blood-vessels is associated at the commencement of the process with an **acceleration** in the flow of blood, which, however, rarely lasts more than an hour, except in the outlying parts, and is **followed by** a considerable **retardation** in the circulation, the vessels still remaining dilated.

Pulsation is now evident in the smallest arteries ; and the stream is slow enough to allow the observer to distinguish individual corpuscles in the capillaries and smaller veins—perhaps even in the arterioles.

It has, however, long been known that the acceleration of the blood-flow in an injured part—the so-called *determination of blood*—is not constant, and often subsides without the occurrence of any of the characteristic phenomena of inflammation. Cohnheim considered that *dilatation* of vessels *with increased velocity* of the blood-current ensuing immediately after the infliction of an injury is accidental. In some

* With certain irritants, as ammonia, a short contraction of the arterioles may be the first result.

cases it is followed by contraction, after which *dilatation with diminished velocity* commences. This, on the other hand, comes on slowly, is constant, and persists as long as the cause. *Dilatation with diminished velocity* must be regarded as the essential vascular change of the inflammation.

Returning to the observation of the frog's mesentery—the retardation of the circulation in the dilated vessels is sometimes seen to take place somewhat suddenly, and is usually first observable in the veins. As the stream gets slower, increasing numbers of white corpuscles are seen in the periaxial stream of the *smaller veins*—rolling slowly along, stopping here and there, and finally coming to a standstill. Thus the smaller veins become lined with leucocytes as with a spheroidal epithelium, often more than one cell in thickness. Some stick in the capillaries. The time at which the change occurs varies. The severer the injury, the earlier this layer of leucocytes is formed. The narrowing of the veins by layers of leucocytes, among which there are no red corpuscles, seems to increase the obstruction to the circulation, which becomes slower and slower, possibly both on this account and because the damage is becoming greater. The red corpuscles, with some white, accumulate in the capillaries, which appear as if distended by a red injection-mass. Actual measurement shows that they may be one-fourth larger than natural. After a time, all onward movement ceases in the capillaries, and their contents sway to and fro with the pulse. This is the stage of **oscillation;** and it is succeeded by that of **stasis**, in which no movement of any kind occurs; but the blood, though stationary, may remain fluid—for as long as three days in the bat's wing. Finally, **thrombosis** or coagulation may take place, but not until the capillary walls are dead. Thrombosis puts an end to that escape of corpuscles from the vessels which will be treated of in the next paragraph.

These changes in the circulation may be thus summarised :—

1. **Dilatation** of small arteries, then veins, and lastly capillaries.
2. **Acceleration** of blood-current, quickly followed by gradually increasing
3. **Retardation** of blood-current—first observed in veins—and simultaneously with this,
4. **Leucocytes** in large numbers fall **into periaxial stream**, and lag behind.
5. **Pulsation** in smallest arteries, **oscillation** of blood-stream, and perhaps **stasis.**

2. **Escape of Fluid and Blood-Corpuscles from the Vessels.**—The circulatory and vascular changes have been described as if they were the only phenomena of inflammation. But this is far from being the case. Soon after the veins become lined by white corpuscles, the field becomes more and more obscured by the presence of small round cells in the substance of the mesentery. At even an earlier period, though the microscope does not show it, the fluid which naturally escapes from the vessels increases greatly in quantity, and changes in quality. As soon as the lymphatics become unable to

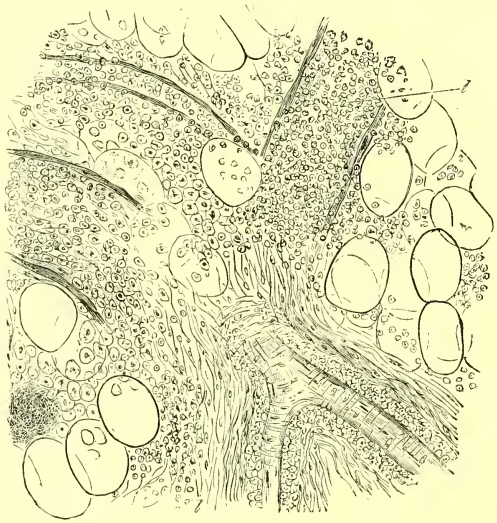


FIG. 104.—*Subcutaneous Tissue some distance above dead part in a Case of Spreading Gangrene.* Three veins packed with leucocytes (*l*), which are escaping freely. Round the artery (below) there are none. Outside the vessels many larger cells are seen. × 200.

carry it off, it accumulates in the connective-tissue spaces, and causes swelling. These finally become insufficient to hold it, and it therefore escapes on the surface together with a number of the small round cells. Here a coagulum forms, consisting of fibrin, small round cells, and some red blood-corpuscles. This **false membrane** can be removed, and the field cleared for observation, until another membrane forms.

a. **Source of the New Cells.**—If a small vein lined by leucocytes be carefully watched, the following changes will be seen—perhaps at once, perhaps not for some time. Some of the leucocytes immediately

adjacent to the wall gradually sink into it, and pass through into the surrounding tissues. Various stages of their passage may be observed. At first, small button-shaped elevations appear on the outer wall of the vessel. These gradually increase until they assume the form of pear-shaped bodies adherent by their small ends to the vessel-wall, often sending out processes whilst so attached. Cornil and Ranvier say that if an adherent leucocyte is torn from the wall and swept on, the adherent part is "fingered," and von Recklinghausen has described the part *within* the vessel (in a tadpole's tail) as sending out processes. Ultimately, the small pedicle of protoplasm gives way, and the passage is complete, the corpuscle remaining free outside the vessel. A similar escape takes place, but to a less extent, from the capillaries.

As a rule in inflammation the escape of white corpuscles greatly exceeds that of the red; but in the most severe cases, in which stagnation is induced in a large number of capillaries, the usual state of affairs may be reversed (Fig. 112, p. 287). From such capillaries the red corpuscles pass out in great numbers, occupy the interstices of the tissues, and give the exudation a hæmorrhagic character. On the other hand, when "retardation" has not culminated in "stasis," most red corpuscles remain within the vessels and pass along through the inflamed area, whilst the white adhere to the walls. The intensity of the injury and profusion of capillaries determine the proportion of red corpuscles in an exudation. These pass out chiefly from the capillaries, and several may escape in quick succession from one place, giving rise to a red spot, visible to the naked eye as a punctiform hæmorrhage. No rupture of vessel occurs, as may be shown by injection.

Both red and white corpuscles at first remain near the vessels whence they have escaped; but they are soon pushed away by other corpuscles, or washed on by the escaping fluid. The white corpuscles have in addition their own peculiar power of locomotion. Thus they may ultimately be found far from their place of egress.

But are white blood-corpuscles the only source of the numberless round cells which crowd the tissues in every inflammation but the most trivial? Virchow advanced the view that they all arose by multiplication of connective-tissue corpuscles. Addison, in 1842, inferred from his observations that leucocytes passed through the vessel-walls and became pus-cells; and, in 1846, Waller actually saw them escaping. These observations were unheeded until Cohnheim, in 1867, asserted that all new cells, formed in the tissues as a direct result of injury, were escaped white corpuscles which had migrated to

the spot where they were found. And, in spite of opposition, this view has held its ground; and all arguments and experiments, advanced to show that the small round cells of *acute* inflammation are due to the multiplication of fixed tissue-cells, have proved inconclusive. Experiments have amply shown that migration of leucocytes will give rise to all the appearances noticed; but it is difficult to exclude the *possibility* of the multiplication of the fixed cells.

Cohnheim, however, believed that the subsequent regeneration of tissues was also due to the development of leucocytes; but this part of his conclusions is now generally disputed.

The following method has been adopted to show that leucocytes *can* produce an infiltration of tissue with small round cells without the aid of the *fixed* elements. A cornea, or other piece of tissue, the cells of which were suspected of multiplying is excised, kept for some days, rendered aseptic, and then placed in the peritoneum or subcutaneous tissue of a living animal. On subsequent examination clumps of small round cells are always found in positions normally occupied by tissue-corpuscles; but multiplication of the latter, which were presumably dead, was clearly impossible. The *fixed* connective-tissue cells lie in spaces and clefts, and the *migrating* cells, taking the easiest course open to them, invade and accumulate in these spaces and around the fixed cells.

The non-vascular tissues, and especially the cornea, were the last strongholds of those who maintained that these cells originated from multiplying connective-tissue corpuscles. Böttcher showed that after slight central injuries of the cornea with nitrate of silver, which caused no affection of the surrounding vessels, the sites of the corneal corpuscles in the neighbourhood were occupied by clumps of embryonic cells which he believed could have been formed only by multiplication of the fixed cells. Cohnheim pointed out that the new cells might be leucocytes which had migrated from the conjunctival sac; and Senftleben proved that this was their source. This observer succeeded in applying to a minute spot in the centre of the anterior surface of the cornea, a solution of chloride of zinc, which soaked through the dense anterior corneal lamina without destroying it. By this method he found it was possible to kill the corpuscles in a small central area of the cornea without affecting the marginal vessels. The spot remained clear, and no clumps of embryonic cells were found. But if the spot irritated was near the margin of the cornea, the neighbouring vessels dilated and the damaged area became cloudy from infiltration with

leucocytes. If to the slight central injury, first described, a cut or stitch through the anterior lamina was added, opacity of the cornea and infiltration of corpuscles from the conjunctival sac occurred simultaneously. It seems therefore that Cohnheim was right in supposing that the small round cells found in inflamed tissues, as a direct result of the injury which caused the process, were escaped leucocytes. A few of the cells may be due to *degenerative* changes (p. 30).

Moreover, in the less acute forms we find cells which are formed by *regenerative* processes going on in the cells of the tissues; but these can and must be sharply distinguished from those we have been discussing (p. 268).

β. **Exudation of Fluid.**—As before stated, one of the earliest effects of the vascular changes in inflammation is increased exudation of fluid. This was noted in the microscopic examination of the inflamed mesentery, but other experiments show the process much better. Lassar tied a cannula into a large lymphatic of each hind leg of a dog. He then stopped the circulation in *one* leg, and dipped this into water at 130° F., thereby exciting acute inflammation. On removing the fillet the lymph-stream from the cannula at once exceeded the normal, and soon reached *eight times* that on the sound side. At first the fluid was clear; but after a time increasing numbers of white corpuscles made it cloudy, and red corpuscles were also found in small numbers. Swelling of the foot began while the flow of lymph was free, evidently because the exudation was too rapid to be conveyed away by the lymph-channels, even when fully dilated. Later in the experiment the flow diminished, partly because exudation diminished as pressure on the vessels (from effusion beneath the skin) rose, and partly from coagulation in, and consequent blocking of, lymphatics. The lymph collected differed from the exudation-fluid in mechanical hyperæmia in containing a much larger proportion of albumin, and in having a much greater tendency to coagulation. This latter property varies with the number of white corpuscles which it contains. The lymph differed from liquor sanguinis in containing less albumin and having a slighter tendency to coagulate. The composition of inflammatory effusion, however, is not constant. In the most acute inflammations it contains a large number of red corpuscles; in less severe forms white corpuscles are greatly in excess of red. In the more severe inflammations the fluid approaches plasma in its composition and tendencies; whilst in the less severe it becomes very like the fluid in mechanical hyperæmia. It also varies according to the part from

which it comes. A mild degree of peritoneal inflammation will pro duce an effusion containing more proteid matter than a far severer inflammation limited to the leg (p. 220).

3. **Changes in the Inflamed Tissues.** — Inflamed parts are soft, and the component tissues are blurred or altogether indistinguishable. Microscopically, the tissue-elements are at first separated by fluid and obscured by leucocytes and fibrin filaments. The tissue-cells, when not obscured by leucocytes, are either structureless masses from coagulative necrosis or are undergoing fatty degeneration. The tissue-fibres are swollen and indistinct: they ultimately degenerate. Red corpuscles are found in even moderately severe inflammations. The changes in the escaped leucocytes and the actual destruction of tissue will be described subsequently.

We must, however, here point out that **regenerative processes** are sometimes discoverable in the cells of an inflamed area, as the following experiment shows.

When Senftleben (p. 266), with chloride of zinc, destroyed all cells in the centre of a cornea without admitting any white corpuscles to the area, the part remained quite clear, and showed no naked-eye change. But on the third day microscopic examination showed that the corneal corpuscles around the damaged area were shooting processes into it. Nuclei appeared on the processes; protoplasm collected around them; and branched cells formed, which again threw out regenerative processes; and so the corneal corpuscles were completely restored. Had leucocytes been admitted to the corneal tissue, controversy would have arisen as to whether they also did not spring from the cells by multiplication; but, inflammatory phenomena being prevented, the regenerative processes could be studied alone. In other tissues also regenerative processes occur—the more resistant elements endeavouring to make good the loss sustained by the tissue; but such attempts are found mainly in chronic and subsiding inflammations. In these we must be prepared to find evidence of cell-multiplication, which will be more marked, and commence sooner, when the injury is slight. The greater the injury, the *more* marked will be the *degenerative* changes, and the *less* marked the *regenerative.*

THE ESSENTIAL LESION OF INFLAMMATION.— Having thus briefly described the succession of changes which occur in the process of inflammation, we may next consider how an injury produces them. An injury has been held to cause abnormal conditions

of the blood, of the tissues, of the nerves, and of the blood-vessels. On one or more of these it must necessarily act.

There is no reason for supposing that the **blood** is necessarily damaged. We can see that while the circulation round a microscopic inflammation proceeds in a normal manner, any corpuscles entering this region tend to stick to each other and to the vessel-walls (p. 263); but, when they get through the part again, they go on towards the heart quite normally as before. Further, blood drawn from an inflamed area behaves exactly like that from other parts.

The **tissue-elements** are certainly affected in cases due to obvious external injury, and probably in all others, but Cohnheim endeavoured to show that *injury to vessels alone* would give rise to inflammation. He injured the vessels of a part by withdrawing the blood from them and then injecting them with irritating solutions. On allowing blood to flow through the part again, he found that all the phenomena of inflammation ensued. It is therefore possible to produce inflammation by injury of the vessels alone, *if* we can be sure that in this experiment the irritant did not pass through to the tissues and damage *them* as well. Conversely, injury of a non-vascular tissue which does not at the same time affect vessels, is not followed by the phenomena of inflammation (p. 268).

Sensory and vaso-motor **nerves** must often be affected by irritants, and no doubt take their part in producing those variations in calibre and flow which often precede the essential phenomena of inflammation. But as all these latter occur with perfect regularity in a part of which everything except the main artery and vein are divided, nerves cannot be regarded as essential to the process.

There remains, then, only the **vessel-wall**. That this is affected is shown by the facts that the earliest phenomena of inflammation are vascular; that injury of vessels causes these phenomena; that injury confined to non-vascular tissues does not cause them. Further, Ryneck has shown that stasis may be produced in the frog's web in which milk or defibrinated blood is circulating in place of normal blood; and also that in vessels, the vitality of which has been completely destroyed by the injection of metallic poisons, no such stasis can be produced. In all spontaneous inflammations, the cause is probably carried to the part by the blood, acting primarily upon the vessels, and secondarily upon the tissues.

There is no detectable structural alteration of the vessel, however, so Cohnheim spoke of the change as **"molecular,"** and regarded it

as possibly chemical in nature. To cover all that we now know of the escape of fluid and corpuscles, it is necessary to assume that the molecular change not only increases the friction between the blood and the vessel-wall, but also that it renders the latter more "permeable" (p. 220).

EXPLANATION OF THE MICROSCOPIC PHENOMENA.—When **contraction** of arterioles is the first effect of an irritant, it is probably due to its action as a direct stimulant of the vessel-wall; but nothing is really known on this point.

Dilatation with Acceleration of flow may probably occur in two ways. (1) Irritation of a sensory nerve is well known to cause dilatation of the arterioles in its own area of distribution. The action of an irritant not sufficiently intense to paralyse the vessels at once, will stimulate the sensory nerves and cause this *reflex local dilatation.* The arterioles dilate and, the blood-pressure being maintained, a larger quantity of blood is admitted to their capillaries, which cannot dilate proportionally. The blood-pressure in the capillary areas is, *ceteris paribus,* raised in proportion to the increase in the cross-section of the supplying arterioles. Under these circumstances acceleration of stream will accompany dilatation of vessels. The walls of the latter, being uninjured, may contract after such dilatation. (2) But Cohnheim found that the same phenomena occurred in the frog's tongue, after section of everything except the lingual arteries and veins. They are then due, perhaps, to *direct action of the irritant upon the local vascular nervous system,* which maintains a certain "tone" in the vessels even after section of the sympathetic. Dilatation of arteries diminishes the resistance to the flow of blood; injury of endothelium increases it. If the former is in excess of the latter, the above phenomena will occur. They are not seen in severe injuries, nor from the slow action of croton-oil on a part. The acceleration is most marked in the outlying parts of the inflamed area.

Dilatation with Retardation of flow. — Retardation soon follows upon acceleration, though the driving force continues unaltered and no contraction of vessels has occurred. Almost the only conceivable cause of slowing is, therefore, increased local resistance, due to alteration in the vessel-wall. It is one of the results of the **molecular change.** Resistance, and therefore retardation, increases with the alteration of vessel-wall until **stasis** and even **thrombosis** are reached, the latter, in the case of capillaries, probably implying death of the part.

Escape of Contents of Vessels.—Normally, the vessels permit the escape of fluid; for healthy lymph, cerebro-spinal fluid, and the fluid which moistens the pleura, are all derived from the blood. These fluids differ from each other in many particulars. These differences depend on that special quality which we have spoken of as "permeability" (p. 220), and which Heidenhain regards as an active secretory process. Directly an inflammation sets in, the normal fluid of the part is changed in proportion to the intensity of the process (p. 267)—the quantity of albumin rises, the tendency to coagulation increases, and corpuscles appear as already described (p. 265). All this is attributed to a *molecular change*, which renders easier the escape of proteids, as has been shown by injecting solutions of such bodies; though the vessels bore the normal blood-pressure without bursting, even after red corpuscles had escaped.

It is generally stated that heavy particles are drawn into and carried along by the swift, axial stream, and that, when the particles in such a stream are of different weights, there is a tendency for the lighter to be thrown towards the circumference. Thus the leucocytes, being lighter than the red corpuscles, consequently pass into the periaxial stream whenever the current is slowed beyond a certain point. They lag behind because they are in the more slowly moving stream. These phenomena will therefore most readily occur in the slower parts of the blood-current (veins). But this explanation is insufficient, as leucocytes weighted with particles of vermilion act in a precisely similar manner. Many observers maintain that the difference between the specific gravity of the suspended particles and of the whole fluid represents the tendency the particles have to fall out of the stream (p. 226).

With regard to the **migration** or **diapedesis** of corpuscles, the words are ill-chosen as regards the red corpuscles, which can take *no active part* in their escape. Moreover, it is plain that the force which drives out the red corpuscle when lying against the vessel-wall, will act also upon the similarly situated leucocyte. It was formerly thought that these manifested no signs of activity whilst they were within the vessels, but many observers have shown that they do. Further, von Recklinghausen has seen a pigment-cell in an adult frog work its way into a capillary and while there send out processes. He argues from this that a leucocyte can work its way out: at any rate we must admit that leucocytes probably are able to do something towards their escape.

The influence of *intravascular pressure* upon diapedesis is uncertain.

Compression of the supplying artery will generally stop the most active migration. On the other hand, arrest of the heart's action in the tadpole has no such effect. The results of experiments devised to show the effect of vaso-motor paralysis are also contradictory. While in the majority of cases vascular dilatation favours diapedesis, there are many exceptions to the rule. Metchnikoff compares the results of inoculating two guinea-pigs under the skin of the ear, one with tubercle bacilli, the other with the vibrio Metchnikowii: in the first animal, the dilatation will be slight and the diapedesis considerable; in the second, the dilatation will be marked, while there will be scarcely any diapedesis at all. If a frog's mesentery be moistened with a solution of quinine no diapedesis will occur, though from their subsequent behaviour it can be shown that the leucocytes are not paralysed. Has the quinine a repellent action on the leucocytes or does it produce some inexplicable resistance in the vessel-wall? The latter view is opposed to all we know of the phenomena in question; and Metchnikoff accordingly accepts the former explanation, and considers that diapedesis mainly depends on some variable quality possessed by the leucocyte which causes it to seek or to avoid the vessel-wall. Others are inclined to attribute differences in the behaviour of the leucocytes to differences in the chemical conditions in the environment.

Destruction of tissue is due to the damage done by the injury to the elements of the part, to abnormal physical and chemical conditions produced by the exudation, to the peptonising action of organisms, and to imperfect blood-supply in the more advanced stages. It is doubtful whether the leucocytes actually destroy tissue, or whether their only function is the removal of parts which are dead, and of such substances as they may be unaccustomed to encounter.

CLINICAL SIGNS OF INFLAMMATION.—These are, *redness, heat, swelling, pain, and impaired function.*.

Redness and **Heat** may be taken together, as they both depend upon the quantity of blood passing through the part in a unit of time. As a rule, this quantity of blood is increased, the excess being most marked in the early stage of the process, when the part is bright-red and hot. Its vessels are then fully dilated, and the resistance but little increased. As the resistance grows, from more marked molecular change and from pressure of increasing exudation, the quantity of blood passing through the part is diminished. Cohnheim excited inflammation in one foot of a dog, and measured the blood returning

through both femoral veins afterwards. At first the delivery on the injured side was excessive, sometimes more than twice the normal; but when diffuse suppuration or sloughing was induced, the delivery became markedly less than normal. Coldness must accompany such a condition; and such a part will be *bluish* if its vessels are dilated and full, but *mottled or pale* if they are compressed by exudation. In most inflammations the internal and external resistances to the circulation are not sufficient to counterbalance the effect of dilatation, and the blood-pressure is kept up; consequently, the delivery from the veins remains excessive throughout, and the part is red and hot. Both redness and heat may be concealed if normal tissues cover the inflamed part. An inflamed foot may appear to be several degrees hotter than its fellow, but its surface-temperature will never equal that in the rectum. An inflamed pleura is never any hotter than its fellow, and may be colder. The local rise of surface-temperature is due merely to more rapid circulation of arterial blood: excess of heat is not produced in the part.

Swelling, beyond the most trivial, which may be due to dilated vessels, is the result of *exudation of fluid and corpuscles.* It may be entirely owing to fluid, as in hydrocele; or entirely owing to small round cells, the fluid having been absorbed, as in orchitis. It varies in amount with the distensibility of the part, being most marked in such tissues as the scrotum and eyelids, and least marked in bone. When due to fluid (*œdema*) the affected part "pits," unless it is very tensely stretched. Swelling from cell-infiltration is firm, does not pit, and is sometimes called "solid œdema." Swelling may escape detection in cases of slight inflammation, in which the lymphatics suffice to carry away the increased exudation (see above).

Pain is due to *pressure* of the exudation on nerve-endings; perhaps also to *chemical irritation* of them. It varies directly with the sensitiveness and the tension of the part, as well as with the rapidity of the effusion into it, as is seen in acute suppuration in a digital tendon-sheath. It is often throbbing from the increase of tension produced by each heart-stroke. The effect of increase of pressure in producing pain is well shown by allowing an inflamed part to hang down.

Impaired function is due to the fact that every inflamed tissue is injured. It is proportional to the damage of the *essential cells* of the affected part.

VARIETIES* OF INFLAMMATION.—The *process* of in-

* Perhaps "Degrees" would be a better term.

flammation is liable to no important variation, but the *exudations* produced by injuries of different intensity acting for different periods of time upon different tissues, vary sufficiently to permit of a useful classification being made upon this basis. It will be remembered that the first effect of injury upon the normal exudation was to increase the quantity of fluid which escaped from the vessels, and to render it more albuminous. Next, whilst the rise in quantity of albuminous constituents continued, leucocytes appeared in increasing numbers, and the fluid became more and more coagulable. Furthermore, with the leucocytes came a few red corpuscles, and these, in the most intense inflammations, were vastly in excess of the white. These differences in the exudation may be found in passing from the spreading edge towards the centre of an inflammation such as that which constitutes spreading traumatic gangrene. There is no break in the continuity of its production; the passage from serous to hæmorrhagic inflammation occurs gradually and *pari passu* with the increasing intensity of the injury. Consequently, the following "varieties" are to be regarded simply as steps in the process of inflammation due to variations in (1) the resisting power of the tissues, (2) the intensity of the cause, and (3) the duration of its action.

1. **Serous Inflammation.**—*Injury slight.*—As a result of *slight* injury, the normal transudation from the vessels is increased in quantity, and contains excess of albumin, but very few leucocytes. Consequently, it contains very little more albumin than serum (hence the name), and does not coagulate, or at most a few flakes form. The best examples are chronic effusions into serous cavities — the pleura, joints, or tunica vaginalis (hydrocele). In each case the lining of endothelium is not destroyed. An effusion of the same kind occurs also in the substance of a part, constituting "inflammatory œdema" (Fig. 105). Such a part is swollen, "pits" on pressure (unless very tense), and is found to be infiltrated with excess of fluid. When it occurs on a mucous surface, such an inflammation is called "catarrhal." In this case the exudation contains mucin. In impoverished states of the blood, especially when the albumin is diminished, inflammatory exudations are liable to be serous, even when the process is of considerable

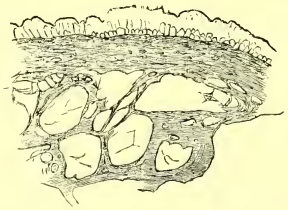


FIG. 105.—*Inflammatory Œdema of Skin.* The large spaces shown were filled with the exuded fluid. (From a specimen by Mr. Boyd.) × 2½.

intensity. In the earlier stages of more intense inflammations, where the emigration of blood-corpuscles is not fully established, as well as in cases where the injury to the vessels, although severe, is rapid and transient in its action (as that caused by heat and blistering agents), the effusion is often a clear and only slightly coagulable liquid. With more severe damage the coagulating power of the exudation increases. Networks of fibrin are frequent in the meshes of inflamed connective-tissue; and large flakes of it may come away in otherwise serous effusions. These inflammations are called **sero-fibrinous**, and lead on to the next class.

Fibrinous Inflammation.—*Injury more intense.*—In this form the exudation is still more richly albuminous and contains more leucocytes; it consequently has a much greater tendency to coagulate, and "**lymph**" forms on the inflamed surface or in the substance of the inflamed tissue. The most typical examples are found on serous membranes. On the surface of the visceral pleura, for example, an irritant produces redness from dilatation of vessels; then follows exudation of fluid and leucocytes, with damage of the endothelial lining and fibrin, forming upon the surface, entangles the leucocytes in its meshes. *Fibrin containing leucocytes constitutes "inflammatory lymph."* The white corpuscles may be very numerous, or only a few may be distinguishable in a granular or obscurely fibrillated matrix. "Lymph" may now form upon the opposed surface of the parietal pleura, which becomes infected from the original focus, and the two patches blend. This is the first stage in the formation of an "adhesion"—*i.e.*, a band of connective-tissue between the two surfaces. "Lymph," formed in exactly the same way, is the temporary uniting medium in healing by the first intention; and it is similar "lymph" which "glazes" the surface of an open wound a few hours after its infliction. In these cases the fluid escapes from the free surface. When it occurs on a mucous surface, such inflammation is called "croupous" or "membranous." A similar exudation occurs into connective-tissue as a result of chronic slight irritation; the fluid is apparently absorbed as fast as it escapes; fibrin probably forms, but it soon disappears, and with it those leucocytes which crowd the tissue; while those parts of it which have been destroyed by the primary injury and the process excited by it, are gradually replaced by proliferation of neighbouring connective-tissue cells. Such an inflammation may end in absorption—some leucocytes wandering into lymphatics and re-entering the circulation, others, together with the fibrin, un-

dergoing fatty changes and forming an emulsion which is similarly absorbed.

Productive Inflammation.—*Injury slight, but long continued.*—In many cases the inflammatory process ends in the formation of new tissue—inflammatory fibrous tissue; and the inflammation is then said to be **productive**. In this case the fibrin present disappears, and the exudation seems at this stage to consist of closely packed leucocytes in a scanty homogeneous matrix. The vitality of these is maintained by vascular loops which spring from the capillaries of the inflamed tissue and penetrate among the cells in all directions: this is **granulation-tissue**. It differs from *inflammatory lymph* in possessing vessels and in having a homogeneous instead of a fibrinous matrix. It derives its name from the fact that on the floor of a healing ulcer, which consists of this tissue, the young cells mass themselves round the apices of capillary loops, all of which project towards the surface; and we thus get the floor made up of rounded projections, about the size of a pin's head, which are called "granulations" (Fig. 111, p. 285). *The plentiful formation of vessels is essential to the changes which this tissue undergoes in the production of connective-tissue.* In healing wounds, new vessels have been found protruding from adjacent capillaries by the end of the second day (Wywodzoff).

To ascertain the exact development of granulation-tissue into fibrous tissue, Ziegler placed chambers, formed of two slightly separated cover-glasses, in the subcutaneous tissue of dogs, and removed them at varying periods. Up to the fifth day they contained round cells—some with one, others with a bi- or tri-partite nucleus; then there appeared cells twice the size of leucocytes, containing a large vesicular nucleus, slightly contractile, and capable of taking particles into their substance. These are called **epithelioid** cells, on account of their appearance, and **formative cells**, or **fibroblasts**, because from them all new connective-tissue develops. As they increased in number those with divided nuclei disappeared, so it is probable that the fibroblasts fed upon degenerating leucocytes. After the twelfth day giant-cells in increasing numbers were found, formed apparently at the expense of cells in their neighbourhood—either by their coalescence, or by their abortive attempts at multiplication. Many giant-cells degenerate, but some may develop into connective-tissue. This tissue is formed thus:—the fibroblasts assume very various shapes—pyriform, spindle, and branched—and are closely packed in a homogeneous intercellular substance. The protoplasm of the fibroblasts either

secretes or is itself converted into a substance which fibrillates. By the union of bundles from different cells and by spread of the process to the intercellular substance, there are formed intercrossing fasciculi of fibres, to which adhere some of the nuclei of the original cells with a little protoplasm (Fig. 106).

Sherrington and Ballance repeated these experiments with this additional precaution, that they only left one small aperture by which cells could enter the space between the two cover-glasses. They agreed with Ziegler that leucocytes were the first cells to enter this space, and that these were succeeded by fibroblasts. They differed from him concerning the origin of these fibroblasts. In some cases, in

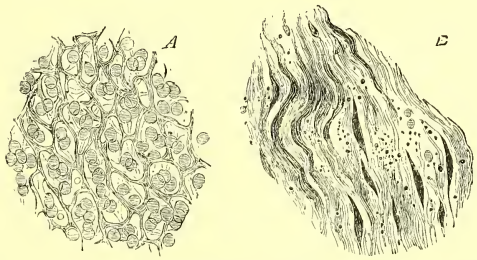


FIG. 106.—*Varieties of New Growth resulting from Chronic Inflammation of Connective-Tissue.* *A*, an *adenoid*, *B*, a *fibroid*, structure. × 200.

less than twenty-four hours after the cover-glasses were placed in position, leucocytes had entered in considerable numbers and had distributed themselves all over the enclosure. But near the point of entry were other cells—plasma-cells, or fibroblasts. These cells differed from the "pioneer" leucocytes in that they were larger, more coarsely granular, and possessed a single clear oval nucleus. In no case were transitional forms seen. The original leucocytes were never observed to undergo any but degenerative changes. The fibroblasts, on the other hand, showed greater power of amœboid movement and of enclosing corpuscles than the original leucocytes. It seems clear that the fibroblasts are the *successors, but not the progeny* of the small round cells found in the earliest stages of inflammation. Sherrington and Ballance consider that the fibroblasts are one of the normal constituents of connective-tissue. Metchnikoff maintains that fixed connective-tissue cells, endothelial cells, and the large mononuclear variety of leucocytes have all the power of developing into fibrous

tissue. The exact origin of the fibroblasts must still be regarded as doubtful. In the meantime it may be observed that the resemblance between Metchnikoff's large mononuclear leucocytes and Sherrington and Ballance's plasma-cells is very close—both in appearance and behaviour. It is worthy of special note that, in the experiments of these last observers, blood-vessels had not developed between the cover-glasses even by the eighteenth day.

The new connective-tissue is called inflammatory or **scar-tissue**. At first it is highly vascular, a recent scar being redder than the surrounding parts; but the tendency to contract is characteristic of this new fibrous tissue, and as this proceeds vessels disappear and the scar, in the course of some weeks or months, becomes white as compared with surrounding parts. This *contraction* of scar-tissue may produce serious results, such as the gravest deformities, or atrophy of the essential epithelial elements of glands (see "Cirrhosis of the Liver"). The contraction is most marked where the tissues are loose, as about the scrotum. It appears to be essential to the process of healing; for this will cease in a callous ulcer of the leg, if infiltration of surrounding tissues and adhesion to deeper parts arrests contraction. A scar is always a weak point in the system, and a tight scar is always irritable and very liable to break down. The tendency of scars is to become fainter.

But granulation-tissue does not always develop into scar-tissue. If the continued irritation become excessive, or the vascular supply be deficient, the process may be arrested at any stage, and degeneration will follow. Deficient blood-supply may be due to insufficient development of vessels, diminution of their lumina (as occur in gummata), or to pressure from too dense packing of the cells. It has been found that imperfect blood-supply is accompanied by the development of giant-cells; they are found in all really chronic inflammations. Thus, the typical structure of a tubercle is—a giant-cell in the centre, surrounded by formative (epithelioid) cells; whilst outside these and intermingled with them is usually found a zone of ordinary leucocytes. (Fig. 107). In gummata and lupus-nodules similar structures are frequent. A section through the thickened synovial membrane in a case of chronic arthritis often shows the following appearances:— Externally, we find ordinary granulation-tissue, with some developing scar-tissue; passing towards the joint-cavity, we find next a layer of formative cells in which giant-cells become increasingly numerous and even typical "tubercles" may occur; yellow spots and

patches of fatty degeneration next become frequent, and the surface may be composed of granular débris in which cell-forms are no longer distinguishable. A fluid, looking like thinnish pus, may occupy the cavity ; it contains, however, very few pus-cells, but consists mainly of fatty granules—formed by degeneration of the superficial cells—suspended in fluid. This is the change known as "**chronic suppuration**" of the knee. "**Chronic abscesses**" of similar nature may form elsewhere, especially in connection with bone (caries of vertebræ). When starting from bone the puriform fluid, formed by

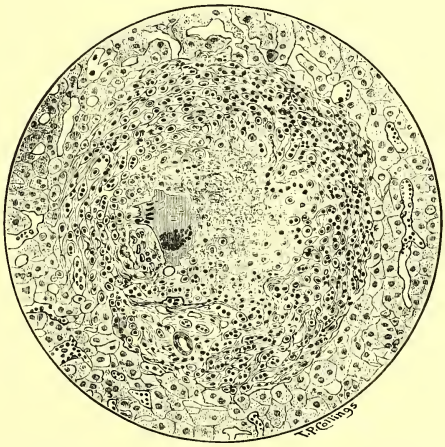


FIG. 107.—*A Tubercle from a Case of Tuberculosis of the Liver.*—A multinucleated giant-cell occupies the centre. Around is an area of commencing caseation and, outside this, a zone consisting principally of fibroblasts, and, to a less extent, of leucocytes. The leucocytes are most numerous on the side where the caseation is most advanced. × 250.

degeneration of the granulation-tissue, simply distends the tissues round about and converts them into a bag, the wall of which yields a little pus. On the other hand, increased irritation will destroy some of the cells of the granulation-tissue and will produce inflammation of it with free escape of corpuscles from its vessels—in other words, will cause it to "break down into pus." This is best seen when a healing aseptic ulcer, with a serous discharge, becomes septic ; the discharge then becomes purulent.

Interstitial is the term applied to inflammations of solid organs, when the manifestations of the process are primarily limited to the

connective-tissue between the essential elements of the organs. Interstitial inflammation may be acute, running on even to suppuration, but as a rule it is an ordinary productive inflammation in which there is but little exudation, and a considerable amount of cell-multiplication. It is accompanied by secondary changes in the essential cells, due to interference with their nutrition. In **parenchymatous** inflammations the epithelial elements of the organ seem to be primarily affected—becoming swollen, finely granular, or even structureless and incapable of staining. These are probably of a degenerative and necrotic nature, mixed up with regenerative processes (pp. 22, 63). The essential lesion of the inflammation must, of course, be of the vessels in the connective-tissue; but the essential cells of an organ are much more delicate than those of its connective-tissue, and show more quickly the effects of a strong irritant, which causes engorgement of the vessels of the connective-tissue and free escape of cells and fluid into intercellular and intra-glandular spaces. Under the action of very slight, chronic irritants, proliferation of connective-tissue cells occurs, with but little or no accumulation of leucocytes. Scar-tissue is thus formed, and the nutrition of the essential cells is more slowly, but none the less surely, interfered with.

Suppurative or Purulent Inflammation.—*Injury intense and prolonged.*—This is a very common form. In it the exudation contains the same elements as in the fibrinous form: the peculiarity of the process is that no coagulation occurs, no "lymph" forms, and no new vessels appear; and even such "lymph" as may have been formed at an earlier stage of the inflammation is destroyed when suppuration sets in. The irritant is more intense than that usually required to produce fibrinous inflammations, and it is essential that its action be prolonged. Serous and fibrinous stages often precede the suppurative, showing that they are minor grades of the same process.

Suppuration may be either **acute** or **chronic**; with the latter we have already dealt. Either of these may appear in a *circumscribed* (*abscess*) (Fig. 108) or in a *diffuse* form, either in the *substance* of a part or on a *free surface*—mucous membrane or skin. In the latter case, when the epithelium is destroyed, with more or less of the subjacent tissues, the process is called **ulceration**; but where the deeper layers of the epithelium remain, it is termed a **purulent catarrh**.

Formation of an Acute Abscess.—When we come to consider the ætiology of acute suppuration we shall find that, in all probability, it is always due to the action upon the tissues of organisms—most

commonly the *staphylococcus pyogenes aureus*. Some of these organisms become arrested in the capillaries of a part, and, *if the conditions are suitable for their growth,* they proceed to multiply and to give off the products of their metabolism. All round them appears a clear hyaline ring of tissue, which does not stain and in which all structure is lost. Obviously some irritant, soaking from the cocci into the tissues, has destroyed the latter and they have undergone coagulation-necrosis. In the course of a few hours a ring of leucocytes appears round this area, and becomes increasingly dense: they infiltrate the necrosed area and press in towards the centre, whilst the cocci, on the

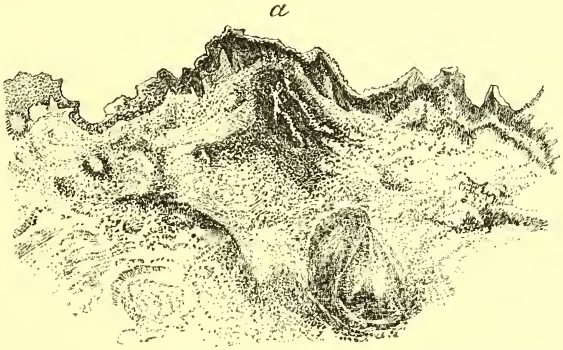


FIG. 108.—*An Abscess in the Skin.* The horny layer has largely disappeared, and the Malpighian layer is pushed upwards by the subjacent abscess (*a*). The mass of pus-corpuscles is just breaking down to form a cavity, the walls of which are thickly infiltrated with similar cells. (Compare Fig. 109.)
(From a specimen by Mr. Boyd.)

other hand, multiply and pass out. The cocci penetrate the tissue in all directions, lying especially in lymph-spaces, and everywhere a layer of leucocytes is formed to oppose them—at first in vain (p. 297). However, after many leucocytes have been either killed by the chemical products of the organisms in the tissue, or starved by the inaccessibility of the necessary nutriment, the resistance to invasion becomes successful and by degrees the cocci are completely walled in by granulation-tissue which everywhere intervenes between them and the healthy tissues. In rabbits, after injection of cocci subcutaneously, the limitation begins on the third or fourth day, but is not complete on the average till the ninth: in man it usually occurs more speedily. At first a central yellowish mass of necrosed tissue infiltrated with

cocci and leucocytes is found, surrounded by the layer in which cocci and leucocytes are struggling for the mastery. Gradually the central mass softens, and it is noticed that the tissue-elements swell up and become indistinct as the cocci spread among them: moreover, no fibrin forms in the fluid exudation. All this is attributed to a peptonising action of the cocci which is acknowledged to be very energetic. So long as the process is actively spreading no new vessels form, but as soon as the leucocytes have got the upper hand vessels appear, and "granulation-tissue" is formed. Thus is developed a cavity, bordered by tissue infiltrated with living cells. This cavity contains dead leucocytes, destroyed and liquefied tissue, and exudation, as well as a

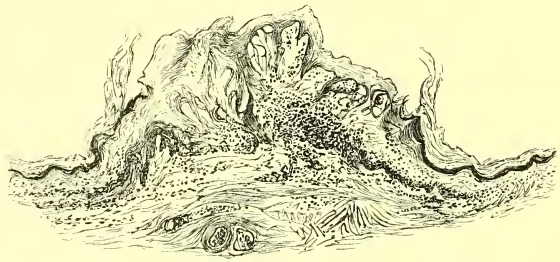


FIG. 109.—*Section through a Small-Pox Pustule.* The horny layer over the centre of the surface has disappeared, and the free edges are shown. A mass of cells is seen in the boundary between the swollen Malpighian layer and the true skin, making its way to the surface. Thus the actual lesion is situate wholly in the epidermis, while the fluid and cells have passed up from the derma, the track being shown. (Compare Fig. 108.)

(From a specimen by Mr. Boyd.)

few living cells which have recently migrated from the surrounding tissues: this fluid is called **pus**. Once formed, such a cavity either enlarges, or shifts its position, or both. The extension occurs in the direction of least resistance. Its approach is marked by thrombosis of the minute vessels and molecular disintegration of the cells they supply, by migration of corpuscles and by exudation of fluid into the newly formed space. Its progress is not arrested until it reaches some free surface or open cavity, upon or into which it bursts. We find on section of the wall of a spreading abscess all the stages of inflammation—a proof of the prolonged action of the cause. In the centre, necrosis; and, in succession as we pass outwards from this, thrombosis, stasis, retardation of flow—diminishing, and perhaps giving

place to acceleration, before the normal circulation is reached. With hyperæmia exudation increases; much of the fluid is taken off by lymphatics, but the corpuscles accumulate in increasing numbers, and red join the white outside the vessels as the centre is approached. This account explains how it is that we are led to the belief that suppuration has occurred, when we find redness, heat, and œdema developing over a deep-seated swelling.

An acute abscess almost always extends until it bursts or is opened; by either of these means, tension, a great cause of the continuance of the inflammation, is relieved, while the pus and its original cause escape together. If the cavity is completely drained and kept at rest, and putrefaction of the discharges is prevented, all pus-formation ceases. Vessels quickly develop in that part of the round-celled infiltration of the walls, in which this has not already occurred: thus they become lined by granulation-tissue. This grows and blends across the cavity, which is often diminished by some falling in of the walls. Scar-tissue then develops, and thus the abscess is healed (pp. 111, 112).

Diffuse suppuration is exactly the same process going on over a wide area. It is often more intense than when circumscribed, and it is by no means uncommon to find shreddy sloughs in the pus, for the effect of the injury on some portions of tissue is so great as to cause *molar* death. Diffuse suppuration is generally due to the *streptococcus pyogenes*—an organism of which the peptonising power is more intense than that of the staphylococcus, which possibly accounts for the difference in their action (see "Micrococci").

Pus from a simple abscess occurring in an otherwise healthy person, (*laudable* pus), is a thick, creamy, opaque, yellowish-white, slightly viscid fluid, having a faint odour, an alkaline reaction, and a specific gravity of 1030 to 1033. It contains ten to fifteen per cent. of solid matter, of which two-thirds are albumin, and the rest fatty matter and salts, such as are found in blood. On standing, it separates into a dense yellow layer, *pus-corpuscles*, and a clear supernatant fluid, *liquor puris*.

Pus-corpuscles are spheroidal bodies about $\frac{1}{2500}$ inch in diameter. They are semi-transparent, more or less granular, and motionless: they usually contain a bi- or tri-partite nucleus, the segments of which together are no larger than the original nucleus. Such division is therefore regarded as evidence of degeneration rather than of multiplication and of growth.

A small minority of the cells have exactly the appearance of leucocytes, and perform amœboid movements. These are the more recently escaped cells. Acetic acid clears up the cells, and renders obvious the often obscure nucleus (Fig. 110).

It is noteworthy that pus has no power of absorbing sloughs or sequestra; *living* cells are required for this. A bit of bone, even an ivory peg, surrounded by granulation-tissue will be slowly eroded; but it may be in pus for months without losing weight, and suppuration is not likely to cease until it is removed. The prevention of suppuration is therefore to be aimed at in all cases of necrosis, and of foreign bodies (especially absorbable ligatures) retained in wounds.

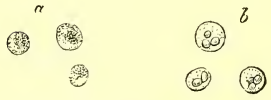


FIG. 110. — *Pus-corpuscles as seen after death.* *a*, Before, *b*, after, the addition of dilute acetic acid. × 400.

Sometimes, though rarely in the case of an acute abscess, after a collection of pus has formed, the irritation diminishes so much that granulation-tissue forms round the fluid, and develops into fibrous tissue. Such pus may long remain encapsuled, its corpuscles breaking down into fatty débris; but as a rule the fluid part is absorbed, and a more or less dry, cheesy-looking mass, consisting of cell-débris and cholesterin crystals, is left in the capsule. The mass may calcify. Such collections may lie harmlessly in the tissues for years, and finally become the centres of fresh suppuration. These changes are much more common in chronic abscesses.

Ulcerative Inflammation.—We have seen that suppuration in the substance of tissues produces molecular disintegration of them: as a rule no distinct slough is found in pus. The same molecular destruction eating away the tissues on a free surface constitutes ulceration. Under the action of an irritant the superficial layer of the skin becomes soaked with fluid, and leucocytes escape in numbers from the vessels and wander even into the epithelial cells, where they seem to have arisen by endogenous multiplication. Under these circumstances the superficial cells do not become horny, and are easily brushed off; or the original irritant may have destroyed their vitality and cohesion, and they are washed away by escaping fluid. The rete is now exposed, and the deeper tissues are liable to irritation from slight friction, contact with chemical irritants, or putrid discharges. The inflammatory process becomes more intense, the escape of fluid and leucocytes freer, and stasis and thrombosis occur here and there. Portions of the

papillary layer and of the covering epithelium die, disintegrate rapidly and come away in the discharge. The process spreads by the production of limited stasis and death of tissue; if the stasis is at all widespread, a visible slough will result. It is common, indeed, to see tags of dead tissue adherent to the floor of a spreading ulcer. If the irritation becomes more intense these shreds will increase in size

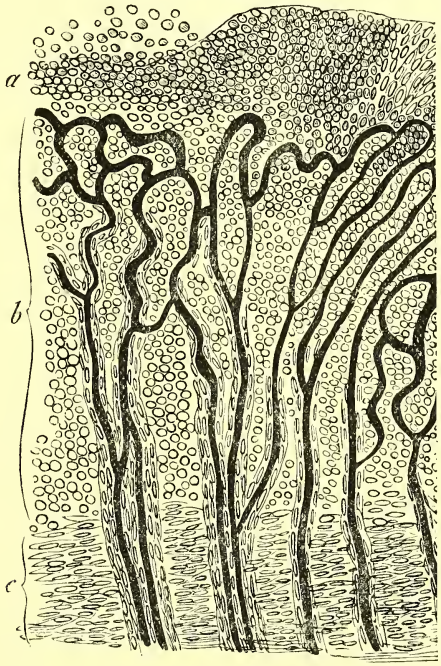


FIG. 111.—*A Granulating Surface.*—*a*. Layer of pus. *b*. Granulation-tissue with loops of blood-vessels. *c*. Commencing development of the granulation-tissue into a fibrillated structure. × 200. (Rindfleisch.) Diagrammatic.

and form "sloughs." Ulceration passes insensibly into gangrene in proportion as death becomes too rapid to permit, by means of degeneration and the action of leucocytes, the molecular disintegration of the parts as they die. The discharge in the spreading stage consists of a few leucocytes and the débris of broken-down tissue suspended in fluid. Like the edge of advancing suppuration, the margin of a spreading ulcer exhibits all the stages of inflammation, from the

mildest to the production of molecular death. An abscess is often described as a closed ulcer. When the causes of the inflammation are removed, the round-celled infiltration of the floor increases and becomes vascularised into granulation-tissue (Fig. 111). Sloughs are detached by the action of leucocytes which eat through their connections with living parts, and the base soon becomes covered with "granulations." When healthy, these are bright-red, slightly raised, rounded elevations, about the size of a small pin's head, and consist of cells grouped round a capillary loop. They contain no lymphatics and no nerves, are not tender, and do not bleed readily. Departure from this type indicates disease of the granulations.

The granulation-tissue grows by multiplication of the deeper cells, and such loss of tissue as has occurred is thus replaced. At the same time the cells infiltrating the edges disappear, and these sink gradually to the level of the base. Epithelium now shoots in from the epithelial cells at the margin, and *three* zones can often be distinguished at this stage:—an inner, dry, *red* zone, where the cells are one or two thick; then a wider *blue* zone where they are thicker, but where no horny cells exist; and lastly, an opaque *white* ring of sodden horny epithelium. The deeper layers of the granulation-tissue are meanwhile becoming scar-tissue, contracting and drawing together the edges of the sore, so that the epithelium has less and less to cover; and finally the whole surface is skinned over, and all granulation-tissue is converted into fibrous tissue. Contraction goes on even after this, and the resulting scar is very much smaller than the original ulcer (pp. 111, 112).

Hæmorrhagic Inflammation.—This form of inflammation is characterised by an exudation in which red corpuscles are in great excess. So far as can be observed, red corpuscles are the latest of all the contents of vessels to escape. In a case of spreading traumatic gangrene, the tissues a *short distance above* the actually gangrenous part were crammed with red corpuscles, showing that the vessels could hold none of their contents (Fig. 112); *higher up* there was a free escape of leucocytes, and of sero-fibrinous effusion (Fig. 104); and *higher still* there was effusion of simple serous fluid only. Of course, the injury may be so intense as to cause an immediate and free escape of red corpuscles from the capillaries. The fluid which soaks the part in these cases is usually thin, and more or less deeply blood-stained. The greater the number of capillaries present in a tissue, the more likely is an exudation to be hæmorrhagic; severity of injury is the

other factor. There are generally many red corpuscles present in the exudation of acute pneumonia. The free escape of red corpuscles shows that the capillary stream in the part is reduced to a minimum, that the injury done to the tissue is a very grave one, and that stasis, death, and thrombosis are impending. Too often gangrene is the termination of such inflammation.

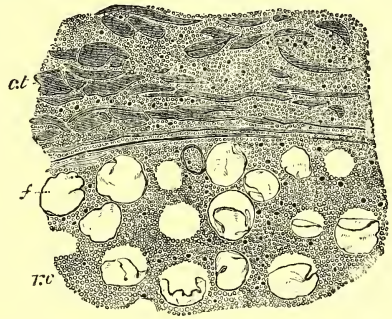


FIG. 112.—*Deeper layer of Cutis and Subcutaneous Fat a short distance above the dead part in a Case of Spreading Gangrene.* The interstices of the tissues are crammed with red corpuscles and a few white. *c.t.* Connective-tissue; *f.* fat cells; *r.c.* red corpuscles. × 200. (Boyd.)

TERMINATIONS OF INFLAMMATION.—These are *resolution, necrosis,* and *new growth.* I. **Resolution.**—This, the most frequent and most favourable termination of inflammation, consists in the cessation of the process and the restoration of the part to health. For this to occur, it is necessary, first, that the exciting cause be removed; secondly, that the walls of the blood-vessels be restored to their normal condition, in order that abnormal transudation may be arrested; thirdly, that all exudation be disposed of; and lastly, that any dead or damaged tissue-elements be regenerated. Obviously this restoration will be more easily effected in the earlier than in the more advanced stages of the inflammatory process. But resolution even of "stasis" sometimes occurs, and may be watched under the microscope. The corpuscles of the stagnant blood move off, one after another, till a slow stream is re-established through the inflamed area. This stream quickens as resistance diminishes, and contraction of the vessels follows the gradual recovery of their muscular coats. Exudation, first of corpuscles, then of fluid, ceases; and the circulation again becomes normal. Serous, sero-fibrinous, and productive inflammations in their

early stages are those which end in *resolution;* but if normal tissue has been once replaced by granulation-tissue or scar-tissue, or has been destroyed by suppuration, ulceration, or gangrene, *resolution* is impossible. A normal condition of the walls of the blood-vessels is dependent upon the proper circulation of the blood through them and their vasa vasorum. Whatever, therefore, favours the re-establishment of normal circulation in the inflamed area will favour resolution.

The last element in resolution is the removal of the inflammatory products—fluid, and corpuscles. These are removed mainly by the lymphatics; but after restoration of the circulation, absorption is carried on to some extent by the veins also. In the later stages of the process any unabsorbed blood-corpuscles or fibrin undergo fatty degeneration, and thus the complete removal of the inflammatory products is much facilitated (see "Grey Hepatisation"). The process of Regeneration in the various tissues has already been described (p. 101).

All conditions interfering with the lymphatic or vascular circulation, such as the pressure exercised by a large effusion in a serous cavity, or by a richly cellular exudation in a lymphatic gland, must retard resolution. It is generally believed that interference with the *lymphatic* circulation tends especially to prevent absorption, and interference with the circulation in the *blood-vessels* to prevent that restoration of those vessels to a normal condition which is necessary to arrest the continued transudation. Recent observers have, however, shown* that fluid artificially introduced into the pleural cavity is mainly absorbed by the blood-vessels; and it is possible that the absorptive power of the lymphatics has been overrated.

II. **Necrosis.**—Inflammation may terminate in death of the inflamed tissue. Weigert has shown that in all but the slightest forms of inflammation, the inability to stain will reveal cells which have undergone coagulative necrosis (p. 22). In most inflammations the destruction of the tissue-elements is still more marked. *Clinically,* we do not speak of necrosis unless obvious *molar* death of tissue has occurred, as distinguished from the *molecular* destruction characteristic of suppuration and ulceration.

The severer the injury, the longer its period of action, and the feebler the resistance of the tissues, the more likely is necrosis to result. It may be produced in the following ways:—

1. By direct injury to a part producing, by its continued action,

* Starling and Tubby, *Journal of Physiology*, 1894.

inflammatory disturbance of the circulation ending in thrombosis. The tissues are affected by the injury simultaneously with the vessels, and suffer *also* from the interference with the circulation.

2. By an irritant conveyed to a part by its vessels, affecting them primarily, and inducing in them changes similar to the foregoing. The tissues are affected secondarily, both by the irritant and by the circulatory disturbance.

3. By pressure of a neighbouring inflammatory exudation. This strangulates the supplying vessels, as in sloughing of skin from tense œdema, in necrosis of tendons in a whitlow, and in death and degeneration of cells in chronic inflammations. Death is more likely to be produced in this way when the exudation occurs in unyielding parts, especially in bone; here sudden death of an extensive exudation means death of the affected part of the bone and its subsequent separation in the form of a sequestrum (see "Necrosis of Bone").

In all infective inflammations the irritant exercises its deleterious effect upon the cells of the inflammatory exudation and tends to destroy them.

Some causes of inflammation always lead to gangrene—*e.g.*, those of carbuncle, malignant pustule, and hospital gangrene. Such inflammations are sometimes called **gangrenous** or **necrotic.**

The ulcerative process by which a slough or sequestrum is detached has already been described (p. 23).

III. **New Growth.**—Inflammations ending in new growth are the so-called "productive" inflammations (p. 276). For this to occur the inflammation must reach the fibrinous stage, must endure for some time, and must not pass on to suppuration. Moreover, the blood-supply must be plentiful.

ÆTIOLOGY OF INFLAMMATION.—Clinical observation has shown that certain inflammations appear to have obvious causes, such as blows and strains: these are called **simple, traumatic** or **phanerogenetic.** We shall presently see how few inflammations fall entirely under this heading. In the vast majority of instances, no cause is obvious: these may be called **cryptogenetic,** although, of late years, the causes of many such inflammations have been clearly demonstrated.

It must always be remembered, in considering the mode of production of an inflammation, that *there are two factors in the process*—**the cause** and **the tissues** upon which it acts. As in the case of

other morbid conditions, the causes of inflammation are **exciting** and **predisposing**. Sometimes no predisposition is necessary, but often the exciting cause of an inflammation cannot act unless the resisting power of the tissues to the irritant in question has been lowered. This impairment of resisting power is the work of the *predisposing* causes; and it may be either inherited or acquired (p. 13). It is obvious that in cases where predisposition is necessary, the condition of the tissues is as essential to the production of an inflammation as is the presence of the exciting cause: the seed and the *suitable* soil must come together to produce the plant.

With regard to the nature of the exciting cause—it is always some mechanical, chemical, or physical agency. The simple deprivation of blood-supply, which leads to injury of the vessel-walls and the surrounding tissues, is enough. If these agents be of sufficient strength and be continued for a sufficient time, they cause death of the part; short of this, they produce distinct changes towards death (p. 297); and, in their slightest intensity, they act as simple "depressants"—*i.e.*, as predisposing causes of disease. Every condition opposed to the health of the whole or of part of the body will here find its place.

Difficult as it is to discover the cause of many inflammations, we should bear in mind the very obvious fact that *no inflammation ever arises without a cause—simple or complex. If an inflammation spreads, its cause has spread before it; and persistence of an inflammation (chronicity) implies continued action of its cause.*

I. **Simple, Traumatic** or **Phanerogenetic Inflammations.**—These are due to the action of some very evident, injurious agency, such as mechanical violence, caustic and irritating chemicals, excessive heat or cold, electricity strong enough to produce electrolysis of the fluids of the part, or prolonged local anæmia and consequent privation of blood. It is characteristic of inflammation from these causes alone, that it has *no tendency to spread beyond the part originally injured nor to pass on to more advanced stages after the cause has ceased to act.* Every one knows how slight are the inflammatory changes induced by very severe *subcutaneous* injuries, even though bones be broken and the capsules of joints torn; and it is to be hoped that all will soon be equally familiar with the absence of inflammation when similar injuries, *communicating with the atmosphere,* are treated in such a way (antiseptically) as to exclude all secondary causes. In animals the effects of each of these irritants can be accurately studied. Hüter injected a

five-per-cent solution of nitrate of silver, or a similar solution of chloride of zinc into the muscles and other tissues of animals, and thus killed the part acted on. In a large number of the cases no sign of inflammation was found in the surrounding tissues. Other experiments were made by plunging a cautery into a muscle (Hallbauer) and bringing the previously divided skin together over the injured part, antiseptics being used. Only such changes occurred round the eschar as take place in the absorption of a simple infarct and its replacement by fibrous tissue. Here, then, we have examples of the most severe mechanical, chemical, and physical injuries killing considerable masses of tissue, but only giving rise to the slightest forms of inflammation. In each case the action of the irritant, though intense, is localised and of short duration. Certain parts are killed absolutely, and the surrounding, damaged area is a very narrow one. So soon as the moxa has ceased acting, the tissues tend of themselves to recover; hence inflammation excited by such causes as the above reaches its height very soon after the introduction of the irritant, and soon subsides unless some fresh irritant is superadded. This is frequently seen after the infliction and proper treatment of a clean-cut wound by a sharp knife (p. 110). A chemical irritant may enter the body at a distance from the part at which its chief action takes place: thus alcohol taken by the mouth causes cirrhosis of the liver; and turpentine or cantharides, inflammation of the kidneys.

Under this heading come inflammations which are referred to cold and wet—"rheumatic" and "reflex" inflammations. When a man gets conjunctivitis from the action upon his eye of a draught through a keyhole, the relation between cause and effect is easily comprehensible; but, except on the hypothesis of greater delicacy of nerve-tissue, it is not quite so easy to understand why inflammation of the facial nerve should ensue from exposure to cold whilst a great thickness of superficial tissue seems uninjured. But this difficulty becomes much greater when internal organs (lungs, kidneys) become inflamed, apparently in consequence of cold acting upon the surface, or of wet feet. Pneumonia, which appeared to be an example of this, is now almost proved to be an infective disease. In this case, any effect produced by cold can be regarded only as predisposing. We know that surface-cold drives the blood to internal organs and raises the blood-pressure. Can this produce inflammation? Lassar plunged rabbits, shorn of fur, into iced water and thoroughly chilled them; he found changes in all the organs, especially the lungs and liver. In these the vessels were

often greatly dilated, the arteries thrombosed, and the veins surrounded by patches of round cells. When the animals were pregnant, the same changes were noted in fœtal organs. He believed the changes to be due to the irritant action of cooled blood upon the vessels of internal parts. Perhaps something of the same kind may occur in man, and a *locus minoris resistentiæ* must be assumed to explain why the kidney in one case, the lung in another, is affected. Frequent exposure to cold might then be regarded as a cause of chronic nephritis; for the temporary albuminuria induced in some people by a cold bath shows that in them the kidneys may be easily damaged.

It is held by some that *excessive functional activity* is a direct cause of inflammation—conjunctivitis from overwork being the usual example.

Nervous influence, too, called into action by irritative lesions of nerve trunks, is regarded as a direct cause; herpes zoster being the favourite instance out of many which might now be quoted as more or less probable examples. The data are not yet sufficient to decide the question (p. 8).

II. **Cryptogenetic Inflammations.**—In a very large number of the inflammations met with in practice there has been no obvious mechanical, chemical, or physical injury. Until recently the causes of such were obscure, and they have hence been called *cryptogenetic,* a better name than "idiopathic."

In the next chapter evidence will be given which proves that some of these inflammations are due to the action of fungi. These may act either as mechanical or as chemical irritants—essentially, therefore, they produce inflammation in the same way as do the gross lesions which have been mentioned as causes of simple inflammation. But fungi which are capable of growth in the body keep up a *continuous* supply of the products of their life-action so long as the conditions are suitable for their development. The products of different fungi vary enormously in their power of injuring the tissues—some producing actual gangrene, others varied degrees of inflammation. It is for the production of those forms of inflammation which require the *prolonged* action of an irritant that the fungi are so peculiarly suited; for, so long as they can grow, a *continued supply* of irritant is kept up. If the irritant is tolerably intense, some variety of fibrinous inflammation is induced, just as by croton-oil (p. 293); when a strong irritant can also peptonise dead tissue and fibrin, suppuration results. If the irritant is less intense, the early stages of productive inflammation (p. 276)

result, as in tubercle and leprosy. The characteristic lesion of these and some other diseases is a tumour-like inflammatory nodule developed round a spot, at which parasites have lodged, and whence they may spread and infect neighbouring and distant parts. Diseases characterised by these lesions are therefore spoken of collectively as the *Infective Granulomata*, a name signifying infective, tumour-like formations of granulation-tissue.

But it would be a very great error to suppose that the **presence of organisms** capable of producing irritant products is sufficient to cause inflammation. We have already pointed out that the **resistance of the tissues** must always be taken into account; and although we are still probably far from knowing all the conditions which influence these two factors—the germ and the soil—experimental pathology has discovered some of them, often of a most astonishing nature.

The rôle of organisms in the production of inflammation will be influenced by their detention in the tissues, by any local or general predisposition in the tissues, by the anatomical characters of the part and other considerations. These subjects are discussed in the following chapter (p. 323).

Ætiology of Suppuration.—No one now doubts that suppuration is commonly the result of organisms (p. 280); but the question is whether it is always so. There is considerable doubt as to whether certain simple irritants cannot be so employed experimentally as to produce suppuration. Nitrate of silver and similar salts when injected form albuminates and probably soon cease to irritate; but if glass capsules of croton-oil or turpentine, which are not thus neutralised, are placed aseptically in the subcutaneous tissue, and the capsules broken when the wound is soundly healed, suppuration results, and no organisms are found in the pus (Cheyne, Councilman).

Strauss, Klemperer and many other recent observers, on the other hand, using extreme precautions to prevent the entry of organisms along with the needle, have come to the opposite conclusion—viz., that under no conditions do simple chemical irritants give rise to the formation of pus. Cheyne, in summing up the evidence upon the question, concludes that the difference of opinion is due to the fact that the putty-like mass of slowly dissolving dead cells and fibrin, which some observers have called pus, is not regarded in this light by others; and he agrees that true, creamy pus is never seen in Man apart from organisms. He mentions, however, that Grawitz and

Scheuerlen have produced acute, aseptic (free from organisms) suppuration by the injection of cadaverine and putrescine-alkaloids, separated by Brieger from putrid flesh, which are not only irritants but are *also* the possessors of peptonising powers.

The conclusion is that, in practical medicine and surgery, we do not meet with the formation of true pus as a result of the action of "simple" causes.

MODES OF SPREAD OF INFLAMMATION.—Spread of an inflammation implies the previous spread of its cause. Now, it is difficult to understand how any of the ordinary mechanical or physical irritants can advance from the spot at which they first act upon the body; and, although it is conceivable that some chemical irritant, due to a faulty metabolism on the part of a group of cells, might soak from the morbid area into the surrounding tissues and thus excite a more or less progressive inflammation, nothing is known of such a process apart from organisms. An inflammation which is characterised by a tendency to spread will always be found to be of parasitic origin. Clinically, inflammations spread by continuity of tissue, by the lymphatics, or by the blood-path. The third mode of advance, if not also the second, necessitates an irritant in a particulate state, for neither a gas nor a fluid in the blood could cause a patch of inflammation at a distance from the primary focus, but would irritate the tissues generally. *Micro-organisms,* on the other hand, having settled at a spot, can spread thence, very much as in the case of malignant growths. (1) They may push their way along the paths of least resistance as they grow, or be carried for short distances by lymph-streams or by leucocytes which have taken them up—spread of the inflammation by "continuity of tissue" resulting in each case (Fig. 113). (2) They may be carried by the lymph-stream long distances from the primary focus. Conveyed in this way, they are usually arrested in the first lymphatic gland they reach. Here they often excite a secondary inflammation without having caused any trace of inflammation *between* the primary focus and the gland—the organisms passing easily through the lymphatic vessels, but becoming arrested in the sinuous channels of the gland, precisely like the particles of pigment which may be found upon microscopic examination of a gland on the "central" side of any extravasation of blood. (3) The organisms may enter the blood-vessels and be carried about by the blood-stream until arrested, when, under favourable conditions, they

will multiply and give rise to a secondary (metastatic) inflammation, such as we get in pyæmia in almost all organs or parts, and in mumps when the testis or ovary becomes inflamed.

MODE OF ARREST OF AN INFLAMMATION.—The dying out of an inflammation excited by one of the *simple* causes is easily understood. As soon as the causes are removed, the cells of the damaged tissues begin to exert their inherent tendency to recover from injury (p. 15). Dead and dying cells are removed by leucocytes,



FIG. 113.—*Small portion of a Muscle near Shoulder, from a Case of Sarcoma of the Head of the Humerus*, showing passage of small round cells (probably sarcomatous) along the "lines of least resistance," as in diffuse inflammation. Where the cells are thickest the muscle-fibres are obscured or have disappeared.
(From a specimen by Mr. Boyd.)

and their places are taken by new cells springing from the normal tissue-elements. But when once a brood of bacteria has gained a foothold in the tissues and has begun to multiply and spread, the inflammatory process also spreading, *pari passu*, it is difficult to see how the advance is checked. Clinically, inflammations spread rapidly and widely, and yet, perhaps after causing gangrene of a large part of the body, become ultimately arrested. The fact is that all the time there is a struggle for existence going on between the cells of the body and the invading parasites, and the victory may lie with either and may be won perhaps easily, perhaps only after a struggle of which the issue is for long doubtful. It will be remembered that the first

effect of an injury is to cause dilatation of the vessels of a part, and Landerer surmises that this flushing of the part is often successful in sweeping away for destruction or elimination from the system, bacteria which have settled and begun to exercise their noxious influence. If this does not happen, the germs will probably find their way into the tissues and the inflammation will spread more or less. In the case of pyogenic cocci giving rise to an abscess, we have seen (p. 280) that, at first, a zone of coagulative necrosis forms round the microbes, that this is infiltrated by leucocytes from outside and by cocci from within, that it next softens and disappears leaving the leucocytes and cocci more or less mixed up, but that by the eighth or ninth day, sections of the abscess-wall no longer show this *mingling* of the opposing forces —the leucocytes now forming a compact wall round the central fluid (pus) which contains both dead leucocytes and the cocci. Similarly, beyond the edge of an advancing erysipelatous or other spreading inflammation, there appears a cloud of these leucocytes, no doubt exercising a corresponding function. As to the weapons with which the war is waged nothing very exact is known. It may be that the products of the two classes of cells floating in the same nutrient fluid are mutually injurious and that those of the body-cells tend to render this fluid unfit for the growth of the bacteria. Again, it may be that the bacteria, as is usual with living things, secrete or excrete products hostile to their own existence, and that these at last accumulate in such quantities as to check the growth of the organism. But there is another way in which microbes appear to be destroyed about which more facts have been accumulated. It has long been known that micro-organisms, like other particles, are taken up by leucocytes; attention was first drawn to it by Koch in his account of mouse-septicæmia. In his paper on the Ætiology of Tuberculosis, Koch has advanced the view that, as the tubercle bacilli are incapable of locomotion, the commencement of a tubercle is due to the escape from a vessel of a leucocyte which has taken up from the blood one or more tubercle bacilli. He expresses his belief, founded upon numerous observations of microscopic specimens, that this leucocyte soon sickens and swells up, first into an "epithelioid" cell, then into a giant-cell; and that the bacilli are short-lived, not uncommonly dying and disappearing from a cell, but often maintaining their position by the production of fresh bacilli. Metchnikoff has confirmed Koch's observation by a very direct method. He found that a little crustacean, the water flea (Daphnia pulex), suitable for microscopic observation,

was subject to invasion by a fungus, the pointed spores of which penetrate its intestine and enter its tissues, where they are at once surrounded by amœboid corpuscles like leucocytes. The spore swells and ultimately breaks into fragments, whilst the victorious leucocytes blend to form a giant-cell. All this goes a long way towards proving that, under favourable circumstances, leucocytes may take into their substance and destroy these vegetable parasites; and it seems likely that the beneficial effect of moist warmth in inflammation is due largely to the fact that it aids migration, and thus increases the army of leucocytes upon which so much depends.

Phagocytosis.—Mention must here be made of Metchnikoff's explanation of inflammatory phenomena in general. In his opinion, the whole process is the result of an effort made by the invaded organism to destroy any virus that has gained access to it. Thus, the dilatation of the vessels, the increased diapedesis, and the apparent conflict between leucocytes and organisms, are all automatic efforts on the part of the individual invaded, and not, as has hitherto been suggested, the purely passive results of ordinary processes on damaged tissues.

Metchnikoff divides leucocytes into four varieties:

1. Small leucocytes with a single large nucleus. These are found in lymphatic glands in large numbers, and are hence called *lymphocytes.*

2. *Large mononucleated leucocytes.* These are full-grown lymphocytes.

3. Large, coarsely granular leucocytes, with lobed nucleus, staining with acid aniline dyes (*eosinophile cells*).

4. Large, *polynucleated leucocytes,* difficult to stain (except nucleus), and therefore called *neutrophile* cells. These are the most numerous of all.

The members of the second and fourth groups are *phagocytes—i.e.,* they attack and attempt to engulf any organism or other foreign substance to the presence of which they are unaccustomed. The endothelial cells are also phagocytes.

According to Metchnikoff the phenomena of inflammation are directed to bringing the phagocytes into contact with the invading organisms in order that they may be able to enclose and destroy the invaders. Inflammation may thus be either *extravascular* or *intravascular.* The former has already been described at length. By the latter is meant the action of the phagocytes on any foreign particles *in the circulation.* When an inflammation terminates favourably, the

phagocytes survive and the organisms disappear. If, however, the organisms are too powerful for the phagocytes, the latter will die and fall to pieces and the organisms will be set free: this frequently happens in tubercle. Chemiotaxis (chemotaxis) is a term used to express the attractive or repellent influence which the environment exercises over the phagocytes that come under its influence. According as it attracts, or is neutral, or is repellent, it is called positive, neutral, or negative. In conditions of negative chemotaxis the organisms are unmolested and consequently propagate rapidly; but the phagocytes may become proof against this condition and cease to be repelled. In this case the final issue may be reversed.*

CHAPTER XXI.

THE VEGETABLE PARASITES.

Fermentation and Infective Disease.

It has long been thought that the group of acute specific diseases must have a very special cause. The characteristics of this group are: (1) that they occur in epidemics; (2) that they are obviously contagious and infectious; (3) that each member is absolutely distinct from its fellows, and runs a typical course; and (4)—the most important distinction of all—that the poison which gives rise to each of them multiplies in a marvellous manner. Thus the introduction into a community of a single case of one of these diseases may be followed by the death of thousands from the same disease. For a long time nothing could be discovered to account for the appearance of these diseases; though they were obviously produced by something which multiplied in the patient, which clung about his clothing, and which could be carried through the air for considerable distances. This "something" was, and still is, called the "*contagion*" of the disease; and for many years science has been endeavouring to discover its nature. It was soon recognised that no gas would meet the requirements of the case, for diffusion would soon put an end to its power for mischief. A fluid was still more out

* For further information on these points the student is referred to the article on "Phagocytosis," by Sidney Martin, in Quain's "Dictionary of Medicine," 1894, and to Metchnikoff's Lectures on the "Comparative Pathology of Inflammation," translated by Starling, 1893.

of the question. *Contagion* was, therefore, necessarily regarded as a solid in a state of very fine division—*particulate*. This *contagion* is known to be insoluble, because it can be removed from fluids, both by subsidence (vaccine, Chauveau), and by filtration, the poison not passing through the filter. These facts, taken with its power of multiplication, seemed to show that the contagion was some living organism, hence the origin of the *contagium vivum* or *germ-theory* of disease. In 1840, Henle clearly formulated the doctrine that living organisms, probably of a vegetable nature, were the causes of the acute specifics, and supported the view by arguments which have withstood all endeavours to refute them. Since that time an enormous number of researches have been carried on, to some of which allusion will subsequently be made.

Long before 1840, however, it had been noticed that a close parallel might be drawn between an infective disease and a fermentation. It may be presented thus:—

Infection	Addition of ferment.
Incubation	Period during which nothing is noticed.
Fever, outbreak, and course of disease	Rise of temperature, and active fermentation.
Decline of disease	Gradual cessation.
Period of protection from same disease	Addition of more ferment has no effect.

It may be further noted that, except in cases in which yeast was added to the saccharine liquid, the source of the ferment in cases of alcoholic fermentation was as mysterious as was the source of the poison which gave rise to an epidemic of whooping-cough.

ÆTIOLOGY OF FERMENTATION.—The above parallel was generally recognised; and the cause of fermentation, being much more open to experiment than the cause of infectious disease, was investigated first. Many kinds of fermentation were speedily recognised—lactic, butyric, viscous, &c.; and the close relationship of putrefaction to these processes was soon acknowledged. In each of these, organisms were found, and their relationship to the processes has been the moot point between the upholders of the *vital* or *germ-theory* of fermentation, and the supporters of the *physical theory*. Alcoholic fermentation has been used as the type of all.

The Germ-Theory is adopted by the great majority of scientific

men at the present day. According to this view, the Saccharomyces cerevisiæ (yeast plant) is the *cause* of the alcoholic fermentation. Its food is sugar, together with nitrogen and some inorganic materials, which must also be provided; the immediate products of its life-action are alcohol, carbon dioxide, glycerine, and succinic acid. It is supposed that the sugar passes into the cells, which take what they require for their own growth and repair, and throw back into the surrounding fluid the products of their activity. Thus a yeast-cell forms the above-mentioned substances just as a hepatic cell forms the constituents of bile. Organisms which act in this direct way are known as *organised ferments.* But there is another way in which very similar results are produced. Instead of acting directly, the living cell may act only through a "middleman," which always forms the connecting medium between the organism and its characteristic chemical products, but which does not itself undergo any change (p 303). These "middlemen" are known as *unformed ferments.* Thus, the diphtheria bacillus, resident in the false membrane, gives rise to a ferment which, circulating in the blood, produces—mainly in the spleen—the toxic albumoses to which many of the symptoms of diphtheria are due.

The Physical Theory affirms that fermentation is a "molecular motion" transmitted to unstable organic compounds (fermentable substance) by albuminoid particles (ferment) which are themselves the seat of "motor decay" (*i.e.*, are undergoing decomposition). The molecular motion of these particles may initiate, in a large amount of a more stable substance, changes similar to those of which they are themselves the seat. Any portion of the substance to which this molecular motion has been communicated is capable of transmitting it to other suitable material, and thus the ferment *seems* to multiply. The ferment communicates its vibrations to the particles with which it comes into contact, and these again to neighbouring particles, much as a spark causes the decomposition of a train of gunpowder. Bastian says that there is no proof of multiplication other than that which occurs in a sufficiently strong solution of sulphate of sodium when a crystal of the same salt is thrown in.

It is very difficult absolutely to disprove the physical theory. Its supporters admit the frequent presence of organisms in fermenting fluids, but regard them as accidents, or as spontaneously generated, because the same decompositions can, in some instances, be effected in their absence. Thus dilute alcohol, run over wood-shavings or charcoal so as to expose a large surface to air, is converted into vinegar.

But this is no evidence against the ability of the Mycoderma aceti *also* to effect the oxidation as a vital act; and indeed distinct differences exist between the two processes.

On the physical theory, much was made of the fact that spontaneous fermentations are always more or less impure; that is, there are found in the fermenting fluid many germs quite different from those essential to the particular fermentation. Again, organisms exactly corresponding in form were found in fluids undergoing very different decompositions. From such facts it was argued that there was no constant relationship between any one germ and any particular kind of decomposition. The *predominance* of one characteristic form was accounted for by supposing that the conditions, peculiar to each kind of fermentation, either favoured the growth of a certain organism, or originated it *de novo*. But it has now been shown in very numerous instances, that it is possible to obtain a cultivation of *each* of the various organisms found in a fermenting fluid, and to demonstrate that a special decomposition does not occur unless one particular form of germ is present, all other forms being variable and accidental impurities. And it has also been shown that organisms, indistinguishable from each other under the microscope, may give rise to very different chemical products when grown upon the same culture-medium, and may produce absolutely different results when inoculated upon animals of the same species. It is clear, therefore, that similarity of external form does not imply identity.

A pure cultivation of an organism is obtained by transferring a minute quantity of the substance containing it, to some material in, or on which it will grow readily. The transference is generally effected by means of a sterilised needle. Sometimes solid, and sometimes fluid culture-grounds are employed (p. 331). For the present purpose a solid, transparent material is the best. Once placed under favourable conditions the organism grows rapidly. From the *margin* of the patch formed by it, a fresh culture-ground is inoculated with a needle in the same way as before. This process may be repeated any number of times. Germ-theorists believe that they can thus eliminate everything taken from the original fermentation except the organism which is capable of growth; and they have endeavoured to make this still more certain by the addition of further precautions, such as (1) by washing the organism with sterilised water, and other fluids incapable of destroying it, (2) by filtration, and (3) by drying. They show that even after these procedures inoculation of a suitable

substance with the surviving and purified organism still leads to the characteristic fermentation. But it is *possible* that "particles in a state of motor decay" may have been in the first and each succeeding instance inoculated upon the culture-ground with the organisms, and that they, too, may have been practically multiplied by the communication of their molecular motion to the molecules of the culture-ground.*

Nevertheless, germ-theorists have rendered it certain that these "particles in a state of motor decay" adhere so closely to the organism which is constantly present that they are only able to impart their molecular motion to substances in which this organism will grow. For if the organism dies no fermentation occurs.

Moreover, the "particles in a state of motor decay" have never been shown to possess existence apart from organisms. So-called "antiseptics," which are selected on account of their ability to destroy the lower organisms, invariably check the molecular motions of the physical ferments: so also does heat sufficient to destroy organisms. In general terms, the properties of the physical ferments are those of the organisms.

Finally, it has been shown of several fermentations that the thinnest membrane, or the shortest column of fluid, is sufficient to prevent the transmission of these supposed vibrations; that direct contact with the ferment is necessary; and that sonorous vibrations have no influence upon fermentable substances. If a solution of sugar in a test-tube is divided into two parts by a plug of cotton-wool and yeast is introduced into the upper, this part alone ferments, though *fluid continuity is uninterrupted.*

Although the physical theory may be theoretically possible, the progress of discovery has shown that its rival—the vital theory—is the truer one. To accept the physical theory one must set aside a perfectly satisfactory and evident cause (the organisms) and proceed to support one hypothesis by another. We therefore conclude that *all the processes comprised in the terms fermentation and putrefaction are due to the action of vegetable organisms.*

* Innate power of increasing or growing is not conclusive of life. Liebig pointed out that a small quantity of oxalic acid will act upon a very large quantity of oxamide, splitting the latter into oxalic acid and ammonia—one might say that, supplied with suitable pabulum, the oxalic acid increases indefinitely. Baumgarten says, the difference between the chemical changes effected by oxalic acid and by living organisms is that the former acts by *juxtaposition*, the latter by *intussusception;* but this may mean only juxtaposition with internal tissues.

How do these organisms act? The principal views are :—

1. Organisms, like all living cells, require certain materials for growth and repair. They take into their substance the organic and inorganic compounds which are necessarily present in any liquid in which they can grow, and they give back to the fluid the products of their action. These are known as "*organised ferments.*"

2. Certain organisms produce "*unformed ferments*" (p. 300). The chief characteristics of these unformed ferments are: (1) that they seem to act by mere contact ("catalytically"), taking no part in the decompositions to which they give rise; (2) that they act in extremely small quantity; (3) that they do not multiply, but, nevertheless, can transform many times their weight of the fermentable substance, though, ultimately, they become exhausted; (4) that they are soluble, and are always derived from living cells; (5) that they all require water or moisture to enable them to act, some preferring an acid, others an alkaline reaction; (6) that, like the organisms, they act best at a certain temperature; and (7) that while any marked deviation of temperature arrests their action, and any considerable degree of moist heat destroys their properties, they are, when dried, as resistant to all physical and chemical agencies as spores themselves. They are complex albuminoid bodies, and can be extracted by glycerine. Ptyalin, pepsin, trypsin are well-known examples from the human body; emulsin (bitter almond) and diastase (barley) from the vegetable kingdom. It is certain that some bacteria (*e.g.*, putrefactive and pyogenic cocci) form diastatic and peptic ferments, which can be separated from, and act in the absence of, the organisms. Musculus has separated from the Micrococcus ureæ a body capable of changing urea into ammonium carbonate. The organisms of cholera and diphtheria furnish excellent examples of the power of a strictly localised organism to give rise to general changes through the mediation of "unformed ferments."

3. Nägeli has adopted the view to which Liebig seemed tending—that the life and growth of cells is necessary to fermentation, the chemical changes being always due to the transmission of the molecular motions of *living* protoplasm to the unstable compounds around it.

Products of Fermentation.—In all processes bodies are formed which hinder the development of, and ultimately destroy, the organisms which produce them. Thus, the alcoholic fermentation is checked and ultimately arrested by the accumulation of alcohol;

while putrefaction is hindered by the development of bodies like carbolic acid and cressol. It will be remembered that animals produce substances having a corresponding effect — *e.g.,* carbon dioxide.

If the analogy, pointed out on p. 299, between infective diseases and fermentation were strictly true, we might at once infer that these diseases were caused by the growth and life-action of vegetable organisms in the tissues of the body, especially as many low forms of vegetable life have been found associated with such diseases. But no one could accept the conclusion on the evidence of so superficial a resemblance. The same stringent proofs must be afforded in the case of each disease as were demanded in the case of each fermentation. How far these proofs are forthcoming will be shown in the concluding part of the present chapter. We shall now state shortly what is known of the botanical position and life-history of the vegetable parasites of man.

The Bacteria or Schizo-mycetes.

MORPHOLOGY AND LIFE-HISTORY.—The vegetable organisms, which have been found connected with the diseases of man, are all *Thallophytes,* or plants in which no distinction between stem and leaf exists; and, as they are all destitute of chlorophyll, they belong to the class of *Fungi, not* Algæ. The parasitic fungi are of three kinds—**Bacteria** or *Schizo-mycetes,* **Yeasts** or *Blasto-mycetes,* and **Moulds** or *Hypho-mycetes.* The bacteria, besides causing putrefaction and several of the "fermentations," include almost all the organisms which are believed to produce the infective diseases. They are, therefore, by far the most important group.

The **Schizo-mycetes** or **Fission-fungi** are, with very few exceptions, a-chlorophyllous, non-nucleated, uni-cellular organisms. Many of them approach the limits of microscopic visibility, whilst all are very minute.

Form.—In form they may be said to follow, more or less closely, one of three types—the *sphere,* the *rod,* and the *comma.* The *spherical* bacteria comprise those of any shape between a sphere and a cube. The *rod-shaped* bacteria may be short and thick with rounded ends, so as closely to approach an oval; or they may be long and thin with square ends; or they may exhibit any possible combination of these features. The *commas* in some cases are long and thin, in others

short and thick: they differ also in their degree of curvature. *Spiral* and *dumb-bell* forms are less common.

Structure.—Bacteria consist of a peculiar form of protoplasm, *mycoprotein* (v. Nencki), and appear structureless; but it is very probable, from their great resistance to alkalies and dilute acids, that they possess a cell-membrane of some carbo-hydrate allied to cellulose. During the formation of spores, and after the action of tincture of iodine, which stains and causes shrinking of the protoplasm, a fine membrane may be actually seen. It is very elastic, and seems to form the inner layer of a gelatinous envelope, by more or less of which all bacteria are surrounded.

Colour.—Bacteria refract light strongly, and cause turbidity of any culture-fluid in which considerable numbers are present. Apart from artificial staining, a mass of organisms is usually colourless—*i.e.*, white or greyish. Some organisms are green from chlorophyll: others are brightly coloured, red, blue, yellow, &c., the tint being mainly in the envelope. Bacteria are stained with more or less difficulty by several aniline dyes, and many of them may be identified by their special staining reactions. The colour produced is not always uniform. This irregularity generally depends on spore-formation or on degenerative changes. By some, it is regarded as a possible indication of definite structure. Some forms are stained brown by iron salts in water. The starch reaction with iodine is not rare.

Movement.—Single round cells have no movement other than Brownian; but chains and colonies of them are said by Ogston to be capable of locomotion, though this opinion is not generally accepted. The rod-forms have often a mobile and a motionless stage; but some never move—*e.g.*, B. anthracis, B. tuberculosis. In a few cases, when specially stained, one or more cilia-like filaments or flagella have been found. These seem to be connected with the cell-membrane rather than with the protoplasm, thus differing from true cilia. In some organisms one or more flagella are found at one end only; in others, as in the cholera spirillum, they



FIG. 114.—"*Blue Milk*" *Bacilli*—stained by Lœffler's method to show flagella. (From a specimen by Dr. Arkle.)

may grow from both ends; and in a few, among them the typhoid bacillus, they are very fine and are attached all round. By means of these flagella movement is probably effected. No motionless bacterium is provided with flagella; though on many mobile forms none have yet been found. In these, the mode in which motion is produced is unexplained. Certain algæ, larger and higher in the scale than bacteria, move in a similar manner, but have no cilia. Often no reason can be assigned for a change from motion to rest, or *vice versâ*. A good

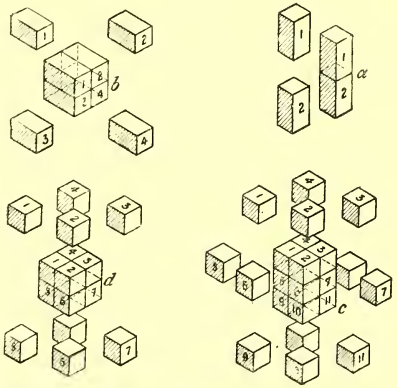


FIG. 115.—*Diagram to show Methods of Reproduction by Fission.*

a. Fission in one direction—the segments lengthening as they divide.

b. Fission in two directions—each segment subsequently divides in the same direction as in *a*.

c. Fission in three directions—in one direction division takes place in two parallel planes.

d. Fission in three directions.

supply of oxygen seems to be connected with the active motion of some forms.

Reproduction.—1. **By Fission**.—All bacteria multiply by transverse division. In the rod-forms, this occurs in a direction at right angles to the long axis. In the spherical forms, it may take place in two or in three directions at right angles to each other. Thus one cell may divide by a single act of reproduction into two, four, or eight equal segments. If two or more parallel dividing planes occur before the separation of the segments takes place, the number of these will be largely and proportionately increased (Fig. 115 *c*). A cell, which divides in a single plane, elongates as it divides, so that the progeny retain the proportions of the original parent-cell.

The first sign of division is the appearance of a fine transverse line crossing the cell, continuous at its ends with the cell-membrane, and often at first imperceptible until stained with iodine—a point to be remembered in estimating the length of apparently single cells.

The new cells formed by fission may at once separate from the parent; or they may for a time remain united to each other, end to end. In this way pairs or chains of cocci and long filaments of rods are formed. A mass of organisms lying side by side in more or less spherical colonies, and bound together by a viscid substance, formed of swollen cell-membrane or of mycoprotein, is known as a *zooglœa.** Zooglœæ often combine to form constant characteristic appearances by which the organism may be recognised—even by the naked eye

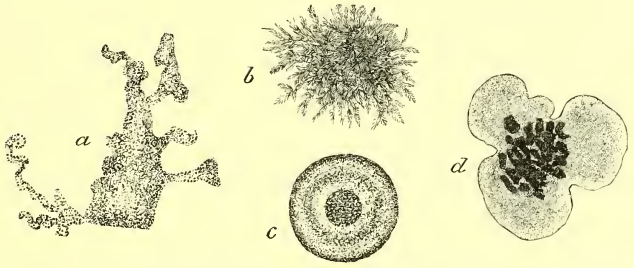


FIG. 116.—*Colonies of Bacteria.* In this figure the enormous difference that may exist between the grouping of one mass of organisms and that of others is shown. (After Sternberg.)

(Fig. 116). Large aggregations of bacteria are always slimy owing to the zooglœæ. The "frog-spawn" coccus (*Leuconostoc*) may fill whole vats in sugar-factories, *Crenothrix Kühniana* and *Cladothrix dichotoma*

* Cocci and micro-cocci . Spherical or nearly spherical.
Diplococci . . . Cocci in pairs.
Streptococci . . . Cocci in chains.
Staphylococci . . . Cocci in groups like bunches of grapes.
Tetrads . . . . Group of four cocci produced by imperfect cleavage.
Sarcinæ . . . . Group of eight or more cocci, similarly produced.
Microbacterium . . Length *not* more than twice breadth.
Desmobacterium . . Length more than twice breadth.
Bacillus . . . . Straight desmobacterium.
Spirillum and vibrio . . Curved desmobacteria.
Spirochæta . . . Flexible, corkscrew, desmobacterium.
Leptothrix . . . Long unjointed thread.
Zooglœa . . . . Group of agglutinated bacteria of any form.
Clostridium . . . Bacillus with transverse projection.
Spirobacterium . . . Curved bacterium.

may block water-pipes and cover reservoirs to a depth of several feet, and a species of *Beggiatoa* covers a large area at the bottom of the Bay of Kiel, called the "dead" ground because fish avoid it: these few examples show how extensive may be the development of zooglœæ.

The time occupied in division has been variously given at from ten to thirty minutes; and, as the offspring proceed at once to divide like their parents, a single bacterium may, in twenty-four hours, give rise to a progeny which Cohn estimates at over 16,000,000.

2. **By Spores.**—Another method of multiplication is met with among the fission-fungi—namely, the formation of spores. Spore-bearing organisms have been divided into two groups—*endosporous* and *arthrosporous*.

The *endosporous group* consists at present of certain long rod-forms (*bacilli*) and some spiral forms, but it is more than likely that spores will be found in species in which they are not now known to occur. The spore forms as a minute point in the cell, enlarging rapidly, and often attaining maturity in a few hours. It is then a clear, round or oval, highly refracting body, which has evidently grown at the expense of the cell-contents: the latter gradually disappear. A spore consists of protoplasm and fat enclosed in a firm capsule. It is quite exceptional to find more than one in a single segment. Spores have often a very close resemblance to vacuoles.

It was formerly supposed that spore-formation was a result of exhaustion of the substratum, and evidence, therefore, of lowered vitality. But it is now known to take place most readily when the conditions of growth are most favourable. Spore-formation in anthrax bacilli can be arrested by reducing the temperature of the organisms below 20° C. or by introducing certain modifications into the culture-ground. Fission and spore-formation may go on together.

The spores are extremely resistant to unfavourable surroundings, owing, apparently, to the qualities of their fine limiting membrane. If after long periods of quiescence they are placed in favourable conditions, germination takes place: their membrane swells, they lose their fine dark outline, and the new vegetative cell grows out in the direction of the long axis of the spore.

In the *arthrosporous group* no spores are found within the cells; but certain cells, during the process of division by fission, exhibit unusual reproductive powers, and are therefore regarded as spores. Sometimes these arthrospores are larger than the rest of the cells: in other instances no difference in appearance can be made out.

As an example of the first variety, the frog-spawn coccus may be chosen. It consists of chains of cells agglutinated into zoogloeæ, and the zoogloea-forms are blended together into irregular masses as large as, or larger than, a hazel-nut. Here and there a cell in the chains becomes larger than its fellows, all of which die. The large cell, if transplanted, germinates.

All micrococci and microbacteria are believed by some to furnish examples of the second variety. No distinction can, however, be drawn between the early and late stages of cocci, and it is better therefore not to include spherical forms among spore-bearing organisms.

Many bacteria are *monomorphic—i.e.,* between their spore and their full development they exhibit only one form—that of their spore. Slight variation in the size and form of the cell is the only variation that such organisms present. Others are more or less *polymorphic—i.e.,* in their life-history spores, rods, filaments, and zoogloeæ can be traced, succeeding each other, or mixed up together.

CONDITIONS OF LIFE AND GROWTH.—Environment.—There is often a marked contrast between the conditions essential to the mere existence of an organism and those which are necessary if it is to grow freely. In this section will be considered the influence which a few modifications in the environment have on the life and growth of organisms taken together. Each variety of fungus seems to differ from all others in its food-requirements, though all must be supplied with the materials whence they can obtain the elements of which they consist. These are carbon, hydrogen, nitrogen, phosphorus, sulphur, calcium, magnesium, and potassium. The first four are generally provided by carbohydrates and albuminoids; the rest by inorganic salts present in animal and vegetable tissues. Certain bacteria, however, can assimilate nitrogen and carbon from much less complex substances than albumin and carbohydrates when these are not available. This is shown by the growth of putrefactive organisms in Cohn's fluid (phosphate of potassium, ·5; sulphate of magnesium, 1; phosphate of calcium, ·05; tartrate of ammonium, 1; water, 100). For the growth of others, the more complex bodies are essential. Thus beer-yeast will not grow unless glucose, or some body convertible into it, is present. It is possible that such a fluid and such conditions could be discovered for each fungus, that it alone would grow in them. Raulin worked out the composition of such a fluid for a mould (Aspergillus niger), and proved the value of each constituent by estimating the

diminution in weight of a specimen of the dried plant, yielded by a certain quantity of the fluid from which the constituent under investigation, had been withdrawn. Very slight differences in the composition of the food-material may favour the growth of one organism more than of another. Nägeli says that in a neutral fluid containing sugar, in which were moulds, yeasts, and bacteria, only the latter flourished—causing lactic acid fermentation; but the addition of *half per cent.* of tartaric acid brought the yeasts to the fore, with the formation of alcohol; while the addition of *four to five per cent.* of the same acid caused the moulds to develop. The **reaction** of the fluid has a marked influence in this respect. As a rule, acidity is unfavourable to the development of bacteria, alkalinity favourable—the reverse usually holding for yeasts and moulds. Very slight differences may suffice to prevent the growth of a bacterium; for example, Koch was unable to produce any disease in *field-mice* with an organism which always produced fatal septicæmia in *house-mice.* Some similar difference would seem to exist between two men exposed to the poison of an acute specific, one of whom catches it, whilst the other does not. A very slight, practically imperceptible, change in the metabolism of the body or of a part may enable organisms to flourish there, even though they were quite unable to do so a short time before.

Many **chemical substances**, are inimical not only to the growth, but also to the very existence of organisms. It has been suggested that the term "antiseptic" should be reserved for those substances which *prevent* their *growth* but which do not cause their destruction; while those which *actually kill* the germs should be called "germicides." But the distinction is not an absolute one. The difference in many cases depends on the degree of concentration. Thus most germicides can be so diluted that they act only as "antiseptics"; though the converse is not equally true.

Mercuric chloride is, on the whole, the most powerful chemical germicide known. A solution of 1:1000 will kill any spores in half an hour. Its power is increased by the addition of salt or of hydrochloric acid (five times as much); while it is seriously diminished by the presence of an albuminous fluid, and absolutely destroyed by the addition of alkalies, and therefore of soap.

A 1:20 watery solution of *carbolic acid* rapidly destroys fully developed bacteria, but takes a few days to kill the more resistant spores. The addition of hydrochloric acid (half as much) increases its germicidal value. On the other hand, anthrax spores have survived

for three months a 1:20 solution of carbolic acid in *oil*. Typhoid bacilli have an unexplained tolerance for carbolic acid. Salicylic acid, boric acid, sulphur dioxide, chlorine, bromine, iodine, and a multitude of other substances have a weaker but analogous action. It is especially worthy of note that while *blood-clot* in wounds is a substance on which most bacteria thrive, *blood-serum* in artificial cultures is distinctly inimical to the growth of many of them.

It will be readily understood that the germicidal power of any substance must to some extent depend:—(1) on the nature of the organism; (2) on the degree of virulence of the particular specimen in question; (3) on any physical conditions that may interfere with immediate contact; and (4) on the presence of any neutralising or incompatible substances. It must be remembered, too, that the rapidity and extent of the effect produced on organisms separated by cultivation from all the constituents of the exudations and secretions in which they are commonly found, as well as from other organisms that may usually co-exist, is no *exact* measure of the effects that will be produced when wounds, cavities, or surfaces of the body are concerned. Neither must it be forgotten that the very substances which are most efficacious in destroying organisms are generally those which interfere most readily with the nutrition of the tissue-cells.

Water.—Nothing that is really dry ferments. The presence of *some* water is essential to the development of all fungi, for it acts as the medium for conveying oxygen and food-substances into the cell. It is easy to add too much or too little for a given species. The moulds require less than the yeasts, and these, again, less than bacteria. Upon jam, dried by addition of sugar, moulds often grow; if less sugar be added, or more water left in the fruit, alcoholic fermentation is common; whilst if the proportion of water be still greater, putrefaction may occur.

Desiccation destroys many vegetative cells within a few days or hours; but many resist drying for months, and spores of the endosporous group do so for years—it is impossible to say how long. Thus, dried cholera spirilla die in three hours, whilst dried typhoid bacilli survive nearly as many months, and diphtheria bacilli longer still.

Oxygen.—Pasteur has divided fungi into two varieties—aërobic and anaërobic. The presence of oxygen is essential to the members of the first group, while it is fatal to those of the second. Aspergillus niger, B. subtilis, and Mycoderma aceti are examples of the first group: the bacilli of tetanus and of malignant œdema belong to the

second. By far the larger number of pathogenic organisms are able to live either with or without oxygen—at least for a considerable time. An organism which thrives *best* in the presence of oxygen, but which *can* grow in its absence, is said to be "aërobic and capably (facultative) anaërobic"; and *vice versâ*. The first of these two groups is the most important, and includes the bacilli of anthrax, tubercle, typhoid, and diphtheria.

Oxygen under pressure may prevent the growth of, and, after months, kill, even *aërobic* organisms. Their spores, also, according to Duclaux, retain their power of germinating much longer if oxygen is excluded: if true, this may partly explain the action of air as a disinfectant.

Temperature.—Each organism flourishes best at a particular temperature. All will grow, but less actively, at temperatures somewhat above or below this point. Now no organism can become parasitic unless the temperature at which it grows corresponds to that of some part of the body to which it finds access. Hence it happens that all pathogenic bacteria grow readily at about the temperature of the human body. In some cases the range within which growth is possible is very limited, as in the tubercle bacillus, which, while it thrives at 99° F. (37° C.), can grow with more or less difficulty at any temperature ranging from 82° F. to 108° F. From this it may be inferred that this bacillus is less likely to exist as an external than as an internal parasite; and that when it does affect the surface, its growth is likely to be slower and its progress more easily arrested. Other organisms, such as those of cholera and typhoid can, in suitable media, grow at a temperature of 60° F. and upwards. These can therefore easily multiply apart from the body. The general statement may be made, with regard to bacteria, that reproduction ceases when the temperature is reduced to 40° F., and in the case of many organisms at a much higher point; but they do not necessarily die. Though rendered rigid and motionless, some can survive extreme cold. The spore-bearing B. anthracis has been frozen in a fluid at – 110° C. without injury; and the typhoid bacillus has survived three hours freezing. The maximum temperature at which bacteria can grow is in most cases between 100° F. and 120° F. By further rise of temperature, rigidity and death are induced—more easily in moist than in dry conditions, and much more easily in the adult than in the spore-form. The reaction and nature of the medium in which the germs are heated has a decided influence. Boiling, and indeed a much lower temperature (140° F.)

than 212° F., will kill the great majority of fungi; but solutions containing spores may need exposure to a temperature of 212° F. for many hours before they are completely sterilised. Thus, Tyndall failed to sterilise a hay-infusion by eight hours' boiling. This prolonged resistance of spore-containing fluids to boiling is explained by supposing that fresh generations of adult organisms are developed after the boiling is over, from spores able to resist that temperature for a long time—a view supported by the fact that such fluids may be readily sterilised if boiled, for a few minutes only, on four or five successive occasions at intervals of several hours.

In like manner alternate freezing and thawing destroys organisms more rapidly than continuous freezing. Typhoid bacilli succumb to this treatment in a month, while they resist continuous freezing more than three times as long.

Some vegetative forms have been found which withstand temperatures higher than those named. Duclaux found some bacilli (*tyrothrix* in cheese), which, when suspended in slightly alkaline fluid, were not destroyed by 100° C.; but in an acid medium were killed in a minute: the spores were not destroyed by 115° C. Other species of spore have been met with, which have withstood a moist heat of even 130° C.

Streaming steam has a more powerful germicidal action than superheated steam. This is probably due to its greater degree of moisture, and its consequently greater penetrating power.

The *dry* spores of the B. anthracis and of the B. subtilis are not destroyed by less than three hours' exposure to 140° C.

Rest.—Fungi flourish better in a still medium than in one whose particles are constantly moving: whilst the B. anthracis divides actively in the blood-stream, many other kinds (micrococcus septicus) seem always to settle before multiplying.

Light.—Light, especially bright sunlight, has a destructive influence on organisms. The rays from the violet end are said to be the most powerful, those from the red end, the least. All organisms do not suffer equally. A few even multiply under the action of light. Recorded experiments on this subject are contradictory. The contradiction may be due to the difficulty in excluding the influence of desiccation, oxidation, and changes in the media in which the organisms are placed. *Combined with these,* light unquestionably forms a valuable means of disinfection.

Soil.—Apart from their degree of moisture and from the presence of other organisms, the influence of most soils on the growth of

pathogenic bacteria does not seem to be marked. *Peat,* however, has a distinctly destructive influence over the organisms of cholera and typhoid fever (Dempster).

These are the essentials by which the **growth** of organisms can be modified. Absence of growth does not necessarily mean death of the organism. If the conditions are unfavourable the cells will not develop; but they may not die. By making a comparatively small change in some of the above conditions, the development, and consequently the action, of any given organism may be prevented. This may often be possible when it is quite out of the question to employ measures powerful enough at once to *destroy* the organisms themselves.

DISTRIBUTION OF BACTERIA IN NATURE.— Where are these microscopic vegetable organisms to be found? A putrid wound swarms with them. Whence do they come? There are three possible answers. 1. They may find access to the body from some outside source. 2. They may exist in the healthy body, developing only under special circumstances. 3. They may be spontaneously generated from the tissues.

1. **Earth, air, or water may be the habitat of germs.**—

(*a*) **Earth.**—The soil is the principal storehouse of organisms. Portions of mould taken from *the surface,* and dropped into a sterilised culture-fluid, invariably infect it. Pyogenic cocci and the bacilli of tetanus and malignant œdema are among the forms usually found. In winter Koch failed to find any organisms, at a depth of one metre, in soil which had not been recently disturbed, which was not formed largely of decomposing material, and into which no unusual soakage of water had occurred.

All solids in contact with air, including the surfaces of animals, have organisms upon them.

(*b*) **Air.**—That dust contains much organic matter is easily shown by combustion: and by artificial cultures it can be proved that some of this is living. It has thus been found that spores of moulds are the commonest forms, then bacilli and their spores, whilst *putrefactive* organisms are *comparatively rare.* Organisms of some kind exist in the air everywhere except away from all life—in mountains above the line of perpetual snow, or on the ocean far removed from land and ships. In such places a sterilised fluid would not ferment, even if left exposed till it dried. But wherever life is found, germs are

found. They increase in number as the population grows and as putrescible material becomes more plentiful. Hesse found that the air in a hospital-ward in Berlin contained thirty times as many bacteria as the air out of doors. In some parts of London it is possible to pour sterilised fluids from one flask into others with the result that but a small percentage will become turbid from the growth of germs; in other parts every flask will be infected. Precautions against infection become more necessary as density of population and imperfect ventilation increase; and it is obvious that in the hospitals of large towns such measures, to be successful, must be most stringent, for here putrefactive organisms will be comparatively numerous.

The air is kept supplied with organisms from the surfaces of objects over which it passes. The dust left as the final result of putrefactive processes is a fertile source of contamination. Perfectly still air becomes pure by subsidence of its germs.

(*c*) **Water.**—All water, except such as comes from a great depth (Artesian wells), contains organisms. Rain-water sweeps the air, and infects the soil with the germs which it carries down. All surface-water is infected from the ground through which it soaks. River-water is exposed to all possible sources of pollution. It is scarcely necessary to add that unless the water contains sufficient organic matter to serve as food for the fungi, no multiplication will take place, and that, sooner or later, the germs will die, though perhaps not for many weeks. The existence of many organisms in a sample of water render much organic impurity probable.

2. **Do Organisms Exist in the Living Body?**—They exist in large numbers on its external (skin) and internal (bronchial and alimentary) surfaces, which are in contact with air. On the **skin** they are most numerous on the *hands*—beneath the nails, and in the folds of skin about the nails; and on *parts provided with hair and large glands—e.g.*, the scalp, axilla, and perinæum. Special care is therefore required to disinfect these parts. Inhaled with the breath, organisms are found in the **larger bronchi;** but the smaller tubes and alveoli are probably free, for Tyndall has shown that the complemental air is pure, as it causes a non-luminous gap in an electric beam thrown across a dark room. Further proof lies in the fact that "medical" empyemata, communicating with the air through the lung, generally remain free from putrefaction, whilst surgical empyemata, following an external wound of the pleura, always putrefy.

With food and drink many living germs are carried into the

alimentary canal. All kinds of fungi swarm in the mouth. They grow fewer as the stomach is reached, for the acid gastric juice is unfavourable to the development of most of them. Organisms are plentiful in the duodenum before the food has become alkaline; and the pancreatic juice swarms with organisms after impure feeding. Indeed, the products of normal pancreatic digestion and those of the ordinary putrefaction of albuminoids are practically the same. Throughout the whole intestine, but varying with the products and stages of digestion, enormous numbers of organisms occur. In abnormal states of the mucous membrane, or in too prolonged retention of intestinal contents, the fungi may multiply and excite irritation, and even poisoning, by the products of their action. Experience shows that, after death, putrefaction begins in the abdomen, spreading from the alimentary canal.

By obtaining pure urine directly from the urethra, Lister showed that a healthy urinary tract is free from organisms.

Bacteria on the skin and mucous surfaces may fairly be regarded as *external* to the body proper—*i.e.*, to the tissues. Organisms are found *in* the tissues in many *diseases:* we have now to inquire whether they exist *in* the *healthy* tissues. There are two routes by which organisms may *reach the tissues.* One is through the *skin;* the other, through the *mucous membranes,* especially the respiratory and the alimentary.

1. The *skin.*—As a general rule uninjured epidermis is impervious to organisms; and in practice, nearly all organisms, that gain access by this means, enter through wounds or slight abrasions. Pustules have, however, been produced by rubbing into the skin a pure culture of the staphylococcus pyogenes aureus. Inoculation in these cases seems to have occurred through the walls of the hair-follicles or the sweat-ducts, as it does in the case of acne pustules.

2. The *mucous membranes.*—If organisms enter by the skin it is *a fortiori* likely that they will also enter by the mucous membranes. To decide this question so far as the respiratory tract is concerned, animals were placed in an atmosphere impregnated with anthrax spores. Anthrax is a particularly suitable organism to use as a test, from the readiness with which it thrives in the normal tissues. In an experiment of Buchner's, out of 66 animals thus treated, 50 died from anthrax. It is unlikely that the organisms were swallowed and absorbed through the wall of the alimentary tract; first, because, while large numbers were found in the lungs, few or none were present in the spleen; and secondly, because out of 33 animals *fed* on

double the proportion of anthrax spores only four succumbed. These experiments not only showed that in the case of anthrax the organisms can gain an entry through both these mucous membranes, but also that the entrance through the respiratory mucous membrane is the more readily effected. In the lung they are probably taken up like carbon-particles, carried to lymphatic glands, and thence perhaps to the blood. It is difficult to deny that in many cases there may have been some slight injury at the point of entry.

When animals are fed on putrid material, living organisms may be found in the urine. This is also the case when a large quantity of washed putrefactive organisms is injected into the circulation. Ordinarily, as above said, fresh human urine is sterile. Many germs, of course, are carried to other organs than the kidney, and are found as yellowish masses in the capillaries; they are unable to thrive in the healthy system, and die and disappear in two or three weeks—often much more rapidly. From the above data it is probable that, under ordinary circumstances, organisms can pass through the mucous membranes of man in small quantities only; and that any which do enter soon die, and do not reach the urine alive.

Experiments have been made to determine whether organisms are habitually present in healthy tissues. Portions of healthy organs have been removed with precautions and placed under conditions best calculated to encourage the growth of any organisms that might be present, as well as to prevent their contamination from any extraneous source. The results have been contradictory.*

The balance of evidence seems to be distinctly in favour of the view that, *as a rule,* no living germs are to be found in healthy tissues. But that the blood may contain living pyogenic cocci is probable from the frequency with which inflammation and abscess result from bruises occurring in depressed states of the system (p. 324), but without any break in the continuity of the epidermis (p. 318). If cocci could ordinarily obtain access to the tissues by means of the vessels, it would be impossible by antiseptic treatment (adapted to prevent the entry of living cocci *from without*) to prevent suppuration of wounds from causes reaching them *from within.*

Again, the rarity with which any collection of putrescible fluid in the body undergoes putrescence (notwithstanding the suitability of the temperature), and the certainty with which by care we can keep

* Watson Cheyne, *Trans. Path. Society of London*, 1879; Mott and Horsley, *Journal of Physiology*, vol. iii.

wounds "sweet," seem to be strongly against the existence of *putrefactive* fungi in healthy tissues. It is certain, however, that if these do gain access they may survive for some hours; so that the putrefaction of removed portions of tissue, usually attributed to want of care, may sometimes have been due to the presence of living germs in those portions at the time of their removal from the body. Again, if a suitable nidus be provided for the development of organisms, they multiply and set up their characteristic decomposition. Thus Chauveau performed *bistournage* of a sheep's testis—*i.e.*, subcutaneous torsion of the organ and its main vessels—in one case *before*, and in another *after*, the injection of septic bacteria *into the blood*. In the latter case, in which the testis presumably contained imprisoned organisms, it broke down into a putrid fluid, and excited much inflammation around. In the former, in which the injected bacteria were shut off from the damaged testis, the organ underwent the fatty changes known as necrobiosis. This is the invariable course when under normal conditions the operation is performed as a method of castration: it seems to show that, normally, organisms are not present in the sheep's testes.

Some organisms, however, seem capable of flourishing in tissues which are perfectly healthy—*e.g.*, the poisons of the acute specifics and the B. anthracis. Even here, there is some very obscure difference between individuals of the same species or of closely allied species, which renders some of them suitable media for the development of certain organisms, whilst others are unsuitable—*i.e.*, more or less predisposition is required even when a species of animal *is liable* to a disease. Thus, some people do not appear capable of contracting the acute specific fevers: children are more subject to acute specifics than adults: Algerian sheep are immune to anthrax: young dogs are easily inoculated with the B. anthracis, but old ones are not. One great difficulty in the experimental study of the infective diseases of man is to find animals which are subject to them. Many organisms will thrive only in some particular tissue or fluid of the body: thus, some multiply in the blood, others in lymph, some in bone (osteomyelitis), others in the cerebro-spinal meninges (epidemic cerebro-spinal meningitis) (see "Micrococci").

To sum up:—Organisms in great variety, but in very varying number, exist in air, water, earth, and on all objects exposed to air, on the skin and on those mucous surfaces which are in contact with air. Organisms can probably pass through the pulmonary and intes-

tinal mucous membranes, but in small number; and such as ordinarily thus enter the tissues are unable to develop, so long as the latter are healthy. The life of such fungi among the tissues is short. It seems to be a very rare thing for them to reach the urine alive. Occasionally an organism which can develop in living tissues, enters. The recipient of such organisms is in more or less danger of disease. Some fungi seem to find a suitable nidus for their development in the great majority of mankind: thus, few are immune to the vaccine-virus. All organisms flourish best in tissues the vitality of which is impaired; some probably cannot develop unless this is the case; and still another group cannot multiply in living tissues at all. Two great divisions (clinical) of organisms are thus obtained:—1. The **Pathogenic**, or those which can invade and multiply in living tissues, almost invariably giving rise to disease. 2. The **Non-Pathogenic** or **Simple**, which can develop only in dead tissue, and are therefore found chiefly on the surface of the body, where sloughs and discharges are common. It is a very rare occurrence for putrefactive fungi to find their way *alive* to an internal slough or putrescible effusion, as they did in Chauveau's experiment (p. 318).

3. **Spontaneous Generation.**—The possibility of organisms originating *de novo* from the molecules of decomposing tissues must be mentioned, but cannot be discussed. The great majority of observers are agreed that there is no evidence that it occurs. They hold that, if a fluid or moist solid be thoroughly sterilised, and placed under such conditions that no organisms can enter from without, no organisms will ever develop.

We conclude, therefore, that organisms found in a putrid wound have entered it *from without*; and that the same is true of fungi found in pathological lesions within the tissues, the organisms having entered by a wound or through a mucous surface. For the present, at least, we must adhere to the belief that neither living organisms nor their spores exist normally in the tissues; and that they are never eliminated alive by an excretory organ or by a wound.

This is of fundamental importance in surgery. If organisms could enter a wound from the side of the tissues, aseptic treatment would be impossible. As it is, we are sure that, if we allow no loophole for the entry of germs from without, our wounds will remain free from ferment-processes. Patients are thus saved from the danger of septic intoxication, of septic infection, of pyæmia, and of other infective diseases (see "Pyæmia and Septicæmia"). Once organisms have

gained access to the tissues, it is extremely difficult to destroy them without also destroying the tissues. Improvement of the general health often enables the tissue-elements to resist invasion successfully (see "Immunity").

Products of Bacteria.—The chemical products which result from the growth of bacteria are both numerous and varied. In most cases they comprise a series of complex changes, which are as yet but imperfectly made out. To a considerable extent they depend upon the nature and amount of the material from which the organism in question derives its nourishment, as well as upon the physical conditions by which it is surrounded. Thus, the cholera bacillus, when grown in weak meat-juice, produces a peptonising ferment, but when supplied with a much stronger solution forms a diastatic ferment instead.

Many products of bacterial action have no pathogenic importance: these we shall not discuss. They include: many *pigments,* suggestive of aniline dyes, and certain fluorescent and phosphorescent effects; many *organic acids,* such as lactic, acetic and butyric, and other allied substances; a few *gases,* including carbon dioxide, marsh gas, hydrogen, and sulphuretted hydrogen.

The chief products of pathogenic importance are: (1) *unformed ferments,* (2) *albumoses,* (3) *alkaloids* or *toxines,* and (4) *caustic substances.*

The relation of these different groups to one another can be readily understood by a reference to the following table. The most striking feature it presents is the general similarity between the products of *proteid digestion* and those of *bacterial action.* The processes are not so similar as they appear at first sight. In the first place the ultimate products are different. In cholera an alkaloid is the final product: in diphtheria an organic acid. Furthermore, the experimental inoculation of animals with the albumoses produced by different organisms, clearly shows that these different albumoses are by no means identical; and that their chemical reactions, so far as at present known, give no indication of their pathogenic effects. Thus, in diphtheria the albumoses cause nerve-degeneration, while the organic acid seems almost harmless. In cholera, on the other hand, the alkaloid or final product seems to be the real cholera poison. So far as is at present known, the formation of an alkaloid by an organism is not necessarily preceded by that of a ferment.

In connection with about one-fifth of all known pathogenic organisms, *ferments* have been discovered. The nature of these has been already described (p. 303).

Albumoses are common intermediate products in the sequence of bacterial reactions. In some cases they are the most virulent of all the resulting compounds. This is so in diphtheria and in snake poison. In anthrax and cholera, on the other hand, they are comparatively of slight importance.

Table Comparing Action of Anthrax and Diphtheria Ferments with those of Pepsin and Trypsin. (Martin.)*

Primary Agent, or Primary Infective Agent.	Ferment or Secondary Infective Agent.	Digestive Products.
Living Cell.	Pepsin.	Syntonin. Albumose { Hetero-albumose. Proto-albumose. Deutero-albumose. Peptone.
Living Cell.	Trypsin.	Globulin-like body. Tryptone (peptone). Leucin and tyrosin. A bitter body.
Bacillus Anthracis.	Anthrax ferment.	Albumose { Hetero-albumose. Proto-albumose. Deutero-albumose. Peptone. Leucin and tyrosin. Alkaloid (base).
Bacillus Diphtheriæ.	Diphtheria ferment in membrane.	Albumose { Hetero- Proto- Deutero- } in the membrane. in the body. Organic Acid.

Among the varied products of bacterial growth are a large number of *alkaloidal substances*. Some of these are harmless, but some are poisonous. The latter are known as *toxines*. Examples of both these varieties may be found in putrefying meat, fish and cheese. They can be easily separated and their nature investigated. The virulence of both anthrax and cholera is due to the formation of toxines.

Fate of Organisms in Living Tissues.—It by no means follows that germs, which have actually entered the tissues, will multiply and give rise to disease. Just as in the case of infective

* Goulstonian Lectures, *Brit. Med. Journ.* vol. i. 1892.

inflammations, so in all other infective diseases, *there are two factors in the production of disease*—the attack of the germs on the one hand, and the resistance of the tissues upon the other (p. 289).

Supposing the conditions to be favourable to their growth, pathogenic fungi differ much in the course which they pursue. Some remain about the spot at which they first settled. Others, with different degrees of rapidity, spread by continuity of tissue. Others, again, are carried along in the lymphatics, settling in them here and there, or passing on until the nearest glands are reached. Another group enter the circulation at once, and are carried in the blood all over the body. Some species remain and multiply in the blood, and, in translucent parts, may be seen in the plasmatic zones of the veins; others, again, require to be deposited from the blood at some spot predisposed to receive them. Escape from disease after exposure to infection is doubtless often due to the deposit of germs at spots other than "weak" ones.

The spread of organisms in the tissues, like that of an abscess, always occurs along the lines of least resistance. Furthermore, it is not necessary that the organisms should *enter* the tissues at all, in order to produce disease. In diphtheria the bacillus is confined to the false membrane: this becomes simply a manufactory of the ferment, which is rapidly distributed throughout the body, giving rise, in the tissues, to the albumoses already referred to. In cholera, too, the bacillus is only found in the intestine, while its products are rapidly absorbed and lead to the well-known symptoms. It is therefore clear that the effects of the action of organisms in the body are very varied. Sometimes they are strictly *local*. A small mass of organisms, by means of its chemical products, excites an inflammatory focus, and exerts a peptonising, caustic, or other action on the tissues in which it lies (Figs. 107, 108, p. 279). The action is limited to invasion of the tissues near the point of entry. Sometimes the action is less strictly local. Such inflammation is called *diffuse*. Occasionally the mere mechanical plugging of the vessels may be of importance. The accompanying figure (Fig. 117), showing the bacillus of splenic fever in the vessels of a mouse's lung, gives an idea of the extent to which this process may be carried.

Sometimes, when the organisms multiply in the blood, or discharge into it the products of their action, the most marked effects are *general*. These consist mainly of fever, wasting, and coma, from the action of substances circulating in the blood, the coagulability of which is

sometimes lessened. In others, again, in addition to the strictly local and general effects, the circulating products attack special parts—as in diphtheria, in which the albumoses cause marked degeneration of certain nerves, and consequent local paralyses. Possibly parasitic fungi also produce some effect by the abstraction of nourishment from their host.



FIG. 117.—*Mouse's Lung; Vessels Plugged with Bacilli Anthracis.*—*a*. Alveolus. *v*. Vein full of bacilli. *c*. Capillary, also full. *br*. Bronchus. × 500. Slightly reduced. (Horsley.)

Reference must here be made to the conditions which influence these two factors—increasing or diminishing the power of the organisms, or the resisting capability of the tissues.

(1) **Arrest of an organism** is absolutely necessary before it can by its metabolism produce *local* irritation and inflammation, for if its products are poured into the circulating blood they become too dilute to effect any local injury. Thus pyogenic cocci have frequently been found in the blood of persons having no abscess. Again, lymphadenitis is much commoner than lymphangitis, not because the glands are more accessible to organisms than the vessels, but because the organisms are more likely to be arrested in the narrower and more sinuous channels of the former. But such arrest is not necessary for organisms which, like those of septic infection of mice, act by pouring into the blood poisons which cause fever and other symptoms. Still, though

rest is only *essential* to the multiplication of *some* organisms, it is *advantageous* to the growth of *all*.

Organisms circulating in the blood may be arrested in one of many ways. Of these the commonest are *embolism, thrombosis, extravasation* of blood from injury, and the *migration* and subsequent death of a leucocyte bearing in its interior one or more living germs—which will occur most easily in parts in which the vessels are distended and the circulation slow (venous congestion). It is conceivable that a germ might escape unaided from a vessel under these circumstances just as a red corpuscle does. Numerous methods have been devised to cause the detention of organisms in capillaries through which they could ordinarily pass—such as mixing them with sterilised cinnabar or potato starch. The result was the impaction of the cocci and the development of inflammation, thus demonstrating the effect of simple arrest of the germs.

(2) **Predisposition.**—Unless there is *predisposition* to suffer from the products of the organisms *thus arrested*, their impaction in vessels may not be sufficient to enable them to excite inflammation. Thus, in rabbits Ribbert found numerous masses of pyogenic cocci in the capillaries of the lung and other organs twenty-four hours after their injection; but all disappeared in forty-eight to seventy-two hours except in the kidneys, where alone abscesses formed. Rabbits are less prone than man to suffer from these organisms: and in them at all events, and very likely in man also, *the predisposition of the tissues must be increased* before these particular organisms (pyogenic cocci) can excite inflammation. The predisposition to suffer from the attacks of organisms is increased by **general depression of vitality**. This may arise from privation, and faulty hygienic surroundings. Depressed vitality is also seen after severe acute fevers, and in alcoholic, albuminuric, and diabetic patients. Among these, trivial wounds often prove serious, and operations should, if possible, be avoided. Pyogenic cocci easily gain access; and cellulitis, boils, and carbuncles result. Among savage races and animals, serious wounds frequently heal by first intention. **Local depression of vitality** may be brought about by any kind of injury, and it is here that the "simple" causes of inflammation chiefly come in as predisponents, rendering the tissues more open to the attack of micro-organisms. It has been experimentally demonstrated that anæmia or mechanical hyperæmia, of a part for some hours enables septic cocci to settle and excite a progressive inflammation. Thus Waterhouse injected staphylococci subcutaneously

into his own scrotum with a negative result. He then constricted a portion of it, until it was purple and swollen, and made a second similar injection. An abscess resulted. The effect of ordinary mechanical injury (*usually slight*) in leading to simple abscess, osteomyelitis, and tubercular disease of joints, has long been known, and it has been proved that such lesions act either by simply depressing the tissues or by causing extravasation of blood, and thus allowing germs which cannot grow in the circulating blood to pass out into the connective-tissue, there to multiply and excite inflammation. Ordinary chemical irritants similarly depress the tissues and excite simple inflammation, and Cheyne points out that strong injections into septic cavities probably facilitate the entry into the general circulation of any organisms which the injections fail to destroy. The injurious effect upon the tissues of strong cold or heat applied directly to a part needs no comment, and Lassar's experiments (p. 291) show the effect, upon internal organs, of cold applied to the surface; and though it is not yet known how the cold acts, we may conclude that it would facilitate the passage of organisms into the tissues of the parts which become interstitially inflamed. These agencies, if they cause recognisable changes at all, excite simple inflammation, and the view that an infective inflammation may, so to speak, be grafted on to a simple inflammation has met with wide acceptance. It would seem, however, that pyogenic cocci and other organisms circulating in the blood do not enter the inflamed area and pass out into the damaged tissues *during all stages* of the inflammatory process: they do so freely until the stage in which leucocytes escape in numbers is reached, when—according to Rinne's experiments—they are no longer to be found in the vessels of the inflamed area. Cocci injected during the formation of scar-tissue are said to enter the vessels of the damaged part in excessive numbers. Thence they may pass out into the tissues, but when the scar is fully formed no such difference is noticeable. The explanation given of these observations is that in the early stage of inflammation the tissues are weakened by the injury and unable to cope with invading organisms, which consequently multiply in them; but in a more advanced stage, when free escape of leucocytes is occurring, the damaged tissues are infiltrated and perhaps replaced by a swarm of healthy active cells and possibly by an antagonistic fluid, both capable of dealing with pyogenic cocci. Scar-tissue again, in its early vascular stage, seems to be of feeble resisting power. It sounds somewhat strange that the early stage of inflammation should give rise to a *locus minoris resistentiæ*

—as regards pyogenic cocci—whilst a later stage does not do so; but Cheyne thinks that it fits in well with the fact that acute osteomyelitis and tubercular disease are often induced by slight injuries—rarely by severe, which seem to excite too much reaction.

(3) The **seat of inoculation** and the **anatomical arrangement of a part** are of importance in enabling organisms to obtain a foothold in the body in two ways: 1. *Certain microbes* can only grow in *certain tissues;* they are harmless unless they reach and settle in these tissues. 2. The *physical characters* of a part have much to do in determining whether an organism will live in it, and what form of inflammation will result from its growth. The bacillus of malignant œdema illustrates both these points. It can grow only in connective-tissue; when introduced into the blood, it sooner or later dies, leaving the animal protected against the disease; but if, whilst it is circulating, a bruise is produced, the bacilli pass out with the extravasated blood into the tissues, commence to grow and thus cause the lesions of the malady. Again, inoculation with this organism at the tip of the tail in cattle has little effect on account of the density and coldness of the part: the intensity of the inflammation increases as the point of inoculation approaches the body, and the reaction may also be increased by raising the temperature of the more distal parts. Sheep, which have loose tissue in their tails, react strongly when inoculated even at the very tip of this appendage: the reaction is diminished by cooling the part. Cheyne showed that the injection of a certain quantity of a cultivation of the Proteus vulgaris into the subcutaneous tissue of the back of a rabbit caused an abscess, but the same quantity in the muscles of the back produced death; and, further, an amount of the cultivation, too small to have any appreciable effect in the subcutaneous tissue, caused an abscess when placed among the muscles. No explanation is as yet forthcoming. The limitation of acute infective osteomyelitis to growing bones is another example of the influence of structure upon disease. A last illustration of this point may be found in the difference between the behaviour of the peritoneum and the cellular tissue to pyogenic cocci. The success of a surgeon who, after an operation, washed out the peritoneum with ordinary unpurified tap-water has been greater than that of any one practising the most rigid antiseptics; but the result of washing out wounds of soft parts, or of bones, has been, on the other hand, extremely unfavourable, acute inflammation often supervening. The explanation given is that the peritoneum has great powers of rapid absorption, so that considerable

quantities of putrescible fluids may be injected together with septic organisms into its cavity, and they will be completely absorbed before putrefaction has time to advance to a poisonous extent; but, if injected in still larger quantity, putrefaction occurs with great rapidity in the unabsorbed fluid, and death from septic intoxication results. Waterhouse showed that if a given dose of pyogenic cocci were suspended in normal saline solution and then injected into the peritoneum, no peritonitis followed; but that if a *tenth* part of the dose were injected *with blood-clot,* septic peritonitis resulted. It is easy to understand that the growth of such organisms may frequently depend upon the immediate accessibility of suitable nourishment (p. 311). It is notorious, moreover, that a chronically inflamed peritoneum with a good many scattered adhesions, stands injury better than a normal membrane, and no proof exists that the lymph-flow from the former is more free than from the latter. Possibly, there are more available phagocytes in this case.

(4) The **number of organisms** which gain entry to the body at any one time is a matter of great importance. At first sight, one might think that the only difference in the results after the injection of 1 and of 1,000,000 pathogenic microbes would be the somewhat slower development of the disease in the former case. It was, however, soon found experimentally that this was not so—except in cases of animals strongly predisposed to suffer from the organism in question; and it was then understood that small numbers of organisms would be destroyed by the tissues before they could produce their products in any quantity, whilst a very large number could not be got rid of with sufficient speed to prevent them from producing more or less poison and thus gaining a greater or less advantage over the tissues. Upon this point Cheyne's own researches enable him to enunciate the following laws:—1. The pathogenic dose of a virus varies inversely with the predisposition of the animal to the disease in question. 2. In animals not very susceptible to a germ-disease, the severity of the disease varies directly, within certain limits, with the dose: a small dose produces no effect, the germs being rapidly destroyed; a larger one causes a local inflammation, the organisms being hemmed in and destroyed more or less speedily by leucocytes; whilst a very large dose overcomes all local limitations, the organisms penetrating into the circulation, producing poisons freely, and causing death from septic poisoning. We cannot with certainty predict the dose necessary to produce any one of the above results, because

predisposition varies greatly even among animals of the same species.

(5) The **virulence of organisms** may usually be increased ("exalted") or diminished ("attenuated") by suitable external conditions: thus, *attenuation* may result from cultivating an organism and allowing long intervals to elapse between the successive inoculations; or from cultivating it at a temperature at which growth is very slow, or upon media containing antiseptics in quantity not sufficient to inhibit growth. *Exaltation* of virulence is less readily produced. In the case of the spirilla of cholera it can be effected by procedures described on p. 344. As these procedures can effect such important modifications in these organisms, it is evident that the body may have to deal with them in states of varying virulence; the weaker the virus the more of it will be required to produce a given effect, and *vice versâ*. The absence of inflammation from wounds treated carelessly or left to nature may sometimes be due to the attenuation of any organisms which may have fallen upon it.

(6) **Concurrent growth with other bacteria** may either increase or diminish pathogenic action, and many facts make it probable that the presence of putrefactive with pyogenic cocci in a wound considerably increases the danger to the patient: for the putrefactive organisms, by their irritant products, destroy the granulation-tissue and open up a way of entry for the pyogenic germs. A corresponding fact, vouched for by Cheyne, is that general tuberculosis is much commoner in cases of joint-disease, complicated with *septic* sinuses, than in cases which are kept aseptic. The presence of pyogenic cocci do not seem to increase the spread of tubercular cavities in the lung, but they certainly intensify the effects of the B. diphtheriæ (p. 366). Again, it is said that an osteomyelitis, due to a mixed infection of the staphylococcus aureus and albus, is of greater severity and of worse prognosis than a case in which only one of these species is present. On the other hand, recent experiments have shown that two microbes growing in the body may successfully oppose each other. Thus, if erysipelas-cocci be injected, both under the skin and into the blood, and if a large dose of anthrax-bacilli be introduced twenty-four hours afterwards, so that a large number of cocci are present at the time of the infection, the anthrax-bacilli will all die out in seventeen to twenty-four hours, without causing even local œdema. Now these two organisms will grow together readily *outside* the body, so it is not clear how their opposition *in* the body is brought about.

(7) Lastly, it is probable that **local** and **seasonal conditions** may act upon pathogenic organisms and thus account for such peculiarities of disease as endemicity, or greater prevalence at certain times and under certain atmospheric conditions.

METHODS OF INVESTIGATION.—I. **Presence of Micro-organisms in Fluids.**—*Simple microscopic examination* may be sufficient to reveal organisms of distinctive form or possessing marked powers of locomotion. No preparation will be necessary beyond mounting a thin layer of blood or other fluid.

Staining is by far the most important method, and it is to Weigert that we owe the introduction of the most suitable reagents—the aniline dyes. Logwood stains many fungi well, but it has no preference for them over animal tissues, and does not therefore make them sufficiently prominent. The aniline dyes most often used are fuchsine, methyl violet, methylene blue, and for photographs especially, Bismarck brown: watery solutions are employed, from one-half to five per cent. Cover-glasses and slides should be cleaned in dilute nitric acid and kept in alcohol; before use they should be heated in a spirit flame whilst held in forceps. The following is the method of procedure. Take two cover-glasses which have just cooled, place a *small* drop of the fluid on one, put the other glass on the top of it, squeeze the glasses gently together, and then glide one off the other, so as to leave a *very thin* layer of the fluid on each. Next set aside both cover-glasses to dry in "air," and then pass them three times through a spirit flame. A temperature of 120° C. should be reached for a few seconds, to precipitate and fix any albuminous material to the glass. If a weak staining solution is used, the cover-glasses must be floated on it, prepared side downwards, for some minutes or hours. A strong solution (two to five per cent.) is sometimes as good, and stains deeply in less than a minute. Pour a little on to the dried cover-glass, leave it for a few seconds, wash with distilled water from a wash-bottle, and dry over a flame. Next warm a slide, and just melt on it a little solid Canada balsam; drop the slightly warmed cover-glass on to this and press it down very carefully.

Certain organisms are distinguished by retaining basic aniline dyes, such as fuchsine, gentian violet, and methyl violet, *even* when they are acted on by a solution of nitric acid (1 in 3), which decolorises everything else, including other kinds of bacteria. After the acid has been washed off, the decolorised parts may be stained with some

contrast-colour—*e.g.*, fuchsine or methylene blue. The chief fungi known to stain in this way are the bacilli of tubercle and of leprosy. B. tuberculosis is now constantly sought for in pus, in sputum, and in urine either for purposes of diagnosis, or to learn the result of treatment.

For the examination of fluids for B. tuberculosis, Gibbes' double stain is the quickest. It consists of two parts of fuschine to one part of methylene blue dissolved in an alcoholic solution of aniline oil.

A method of very general use in the search for bacteria, both in cover-glass specimens and in sections, has been introduced by Gram of Copenhagen. Prepared cover-glasses are soaked for some minutes, and sections for some hours, in Ehrlich's solution of gentian violet,* until they are deeply stained. They are then placed on or in a solution of iodine † until they turn brown (*i.e.*, two or three minutes). The specimens are next washed in alcohol, dried and finally mounted in Canada balsam. Some organisms remain deeply stained, but some—such as the gonococcus and Friedländer's pneumococcus—are decolorised. Eosine or Bismarck brown may be used as a contrast stain. This method of staining often helps to distinguish allied forms of bacteria.

II. **Presence of Micro-organisms in Tissues.**—Thin slices of the tissues to be examined should be placed, as soon as possible after death, in strong methylated spirit or in absolute alcohol. When thoroughly hardened, sections may be cut: these must be very thin. If a freezing machine is used, a thinnish slice of the tissue must be soaked in plenty of water for two or three hours to remove all trace of alcohol, and then put into mucilage for a similar time. The sections are washed and then placed for twelve hours or longer in a one per cent. watery solution of the dye selected, which must always be filtered before use: warmth facilitates staining. Some workers transfer the stained section to a one per cent. solution of glacial acetic acid, then to absolute alcohol, and finally to whatever clarifying agent is employed (cedar oil, xylol, coal-tar naphtha): others omit the acetic acid. Each of these fluids dissolves the dye out of the tissue, and the difficulty is to carry the sections through them rapidly enough. It is best, therefore, at first to take only one section at a time out of the staining fluid. One or two trials will show how long the section must be left in each fluid in order that it may still retain a rather pale colour when it is spread out on the slide. Excess of the clarifying reagent is removed with a

* Saturated alcoholic solution of gentian violet, 5 c.c. ; aniline water, 100 c.c.

† Iodine, 1 grm. ; potassium iodide, 2 grm. ; water, 300 c.c.

piece of clean filter-paper pressed firmly on it. A drop of Canada balsam dissolved in *xylol* is put on the cover-glass, and this is applied: chloroform and benzol-balsam slowly dissolve out the stain, and pure balsam is rather difficult to work with.

If a blue or violet stain has been used, the sections, after washing in alcohol, may be dipped in water for a moment, and then placed in eosine- or carmine-solution for an hour; the tissue-elements acquire a red tint, whilst the organisms remain blue or violet. The sections must now be placed in alcohol. The subsequent stages are the same as before.

To examine tissues for B. tuberculosis or B. lepræ, Ziehl's staining fluid * is the best. A saturated alcoholic solution of methylene blue will also be required, as well as a mixture of nitric acid (B.P.) with two or three parts of water. Place the sections in the fuchsine solution, and leave them in a warm place for at least two hours; then transfer them to the nitric acid solution and leave them until the colour is almost gone; then rinse them in water, and put them into methylene blue for an hour. Now pass them through absolute alcohol and whatever clearing reagent is used, and then mount as before. B. tuberculosis and B. lepræ will appear as red rods on a blue ground; all other organisms present will be blue.

With large and delicate sections it is a good plan to use the glass slide as a section-lifter, pushing it obliquely into the xylol or even the alcohol, and there spreading the section out upon it. Large vessels and plenty of the fluid must be used for this purpose.

With large organisms or with successful contrast-staining a power of 500 diameters, and ordinary illumination, will be sufficient for most purposes; but for the smaller fungi an oil-immersion lens, and a substage condenser of very wide angular aperture, are necessary.

Cultivation of Micro-organisms. — Having determined the presence of organisms in a fluid or tissue, it may be necessary to cultivate them, in order either to study their life-conditions or to separate them from all other species and other matter. Cultivations may be made in fluids or in solids.

In Fluids.—Klebs introduced a method which consisted in adding to a sterile fluid a small quantity of the substance containing the fungus. Under suitable conditions the latter will grow. A small quantity of the culture-fluid may then be added to another flask, and

* Dissolve one gramme of fuchsine in ten c.c. of alcohol, and add a hundred c.c. of a watery solution of carbolic acid (1 in 20).

so on until all vestiges of anything introduced into the first flask with the original organisms must have practically disappeared. If more than one kind of fungus is inoculated, or if in the inoculation of successive flasks contamination from the air or apparatus occurs, it may be impossible to obtain a pure cultivation of one organism.

In Solids.—Koch, therefore, introduced solid, transparent culture-grounds. Clear meat-broths and other fluids are peptonised, and then stiffened by the addition of sufficient gelatine (five to ten per cent.) to render them solid at 65° to 80° F., at which temperature most fungi will grow fairly. Agar-agar, obtained from dried seaweed, is now used (one to two per cent.) to stiffen fluids required to remain solid at temperatures above that of the melting point of gelatine, in order that the life-conditions of organisms at any temperature possible in the body may be determined. Solidified blood-serum and other media are also employed. In all cases the culture-ground must be sterilised by heating to 60° C. (140° F.) for short periods on consecutive days. Transparent culture-grounds are generally employed in one or two ways.

I. **Tube-cultures.**—Fill the lower third of a test-tube with the selected culture-ground; insert a plug of cotton-wool into the orifice of the tube; sterilise according to the method just described, and then set the tube aside to cool, either in a vertical or an oblique position, according to whether depth or surface is required. This and the following details are shown in Fig. 118. To make a cultivation on the ground thus prepared, invert one of the tubes, remove its plug, then with a sterilised platinum wire take some of the suspected liquid and transfer it to the culture-ground, puncturing this with the wire as shown in the figure. Re-insert the plug, and put the tube—the right way up—in an incubating chamber under such conditions of temperature as may be desired.

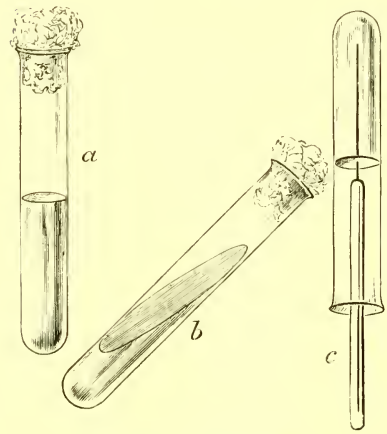


FIG. 118.—*Culture Tubes.*

a. Tube prepared for "stick" culture.

b. Tube prepared for "streak" or "rub" culture.

c. Method of making "stick" culture.

Colonies of organisms will gradually appear (1) on the surface only, if oxygen is essential (aërobic); (2) in the lower part of the track

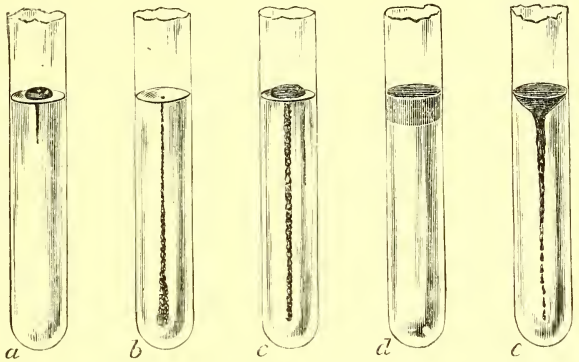


FIG. 119.—*Diagrammatic representation of various Forms of Stick Culture.*

a. An aërobic organism—grows therefore only on surface.

b. An anaërobic organism—grows therefore only beneath the surface.

c. An organism indifferent to the presence of air—grows therefore on and beneath surface.

d. An aërobic organism which liquefies gelatine.

e. An aërobic but capably anërobic organism, which also liquefies gelatine, but in a different manner to *d*.

only, if oxygen is fatal (anaërobic); or (3) on the surface and along the track, if the presence of oxygen is a matter of comparative indifference. In some cases the form of the growth is characteristic (Fig. 120): in others the media are liquefied in some peculiar and therefore diagnostic manner (Fig. 119).

II. **Plate-cultures**—Inoculate a tube as before, warm the medium until it is just fluid, gently agitate the contents, inoculate a second tube from the first, and then a third from the second. Pour the contents of each on to separate glass plates, and keep these in glass-covered chambers under the desired conditions. Isolated colonies will

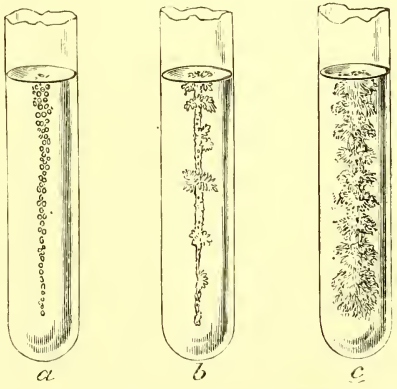


FIG. 120. — *Tube Cultures*, showing peculiarities of growths along the lines of puncture. (After Sternberg.)

gradually develop in different proportions on each plate, and, if very numerous, may run together. Different organisms will produce colonies differing in appearance. Tubes can be subsequently inoculated from whichever of these colonies a cultivation is desired. Thus, for each organism we can ascertain the influence of different temperatures, media and gases, as well as separate one organism from any others that may have been simultaneously introduced.

To examine air, a glass plate covered with gelatine-peptone may be exposed for a given time, and then kept under a moist bell-jar: colonies will grow wherever germs have fallen, and any of them can be subsequently cultivated in tubes. Again, a portion of earth or tissue may be broken up in sterilised water, and a little of this may be shaken with sterilised gelatine-peptone; the latter is then poured on a plate and allowed to set. Most frequently such cultivations are carried on in test-tubes, inoculated with a platinum wire heated to redness just before it is dipped into the substance to be examined. A puncture with it is then made into the gelatine. A very handy method of cultivation is the inoculation of slices of recently boiled potato, made with a pure knife, and kept under a bell-jar in moist air.

In all experiments the apparatus must be carefully sterilised, and each procedure carried on in as still and pure an atmosphere as possible.

CLASSIFICATION OF BACTERIA.—It has already been pointed out that all organisms are by no means of the same shape. Are there sufficient grounds for assuming that because organisms differ in shape, they also differ in species, and that each shape means a different species; or do the many different shapes merely represent different stages in the life-history of a comparatively few species? No classification is possible until this matter is set at rest. The answer is that *form* alone is not sufficient to establish or to disprove identity of species. To obtain satisfactory evidence on this point it is absolutely necessary to watch a given organism pass through its *whole developmental cycle* from beginning to end; to note carefully the form, size, structure, staining affinities, and method of reproduction, of the individual cells in each stage; and to observe their grouping and effects —macroscopic and microscopic—both in the tissues and on various culture-grounds. It is necessary also to discover and separate their chemical products, and to ascertain the effects of inoculation. All these observations must be carried out not only under conditions as natural as can be devised, but also under such as are best calculated to

induce variations. In this way, and in this way alone, can the specific individuality of any organisms be made out, and a useful classification of the different species be devised.

Wherever this laborious investigation has been carried out, no reason has been found to doubt the existence of distinct species of bacteria. And, just as among higher forms, species and even genera, have been confounded with one another until the differentiating points were discovered, so, doubtless, is it with bacteria; and the number of recognised species may therefore be expected to increase continuously. Two coccus-forms may appear to be exactly the same until inoculated upon some particular animal, when marked differences between them will become apparent. Cohn points out an analogy to this in the close naked-eye and microscopic resemblances between the sweet and bitter almond, the chemical constituents and consequent physiological actions of which are so very different; and Virchow alludes to the impossibility of distinguishing between the cells of the early embryo, though their potentialities are so varied. In some of the cases in which bacteria resemble one another in microscopic appearances, in staining affinities, and in culture-effects, differing only in pathogenic results, it is quite possible that the innocuous organism is not a distinct species but only an attenuated variety (p. 328).

Difficulty naturally arose in early times from imperfection in the culture-methods, from inappreciation of the absolute necessity of seeing the development of any given form throughout its whole cycle, and, lastly, from the polymorphism of certain forms which has before been alluded to. The introduction by Koch of solid culture-grounds enabled observers to fix the organisms under examination, and added enormously to the ease and certainty with which pure cultures were obtained; and when it was found that the various developmental stages of polymorphous bacteria were constant both in appearance and in order of succession, it became clear that they were no more disqualified by their polymorphism from specific classification than was the frog on account of its tadpole stage.

In support of the view advanced by Billroth and Nägeli, that all organisms are variations of one or, at most, of a very few distinct species, the following are the chief arguments:—

1. *That in successive cultivations, especially in different media, the forms developed vary greatly from the original; that these assume in succession the shapes characteristic of Cohn's orders;* and that, at the same time, their*

* 1. Cocci; 2. Microbacteria; 3. Desmobacteria; 4. Spirobacteria.

physiological activity changes equally. This is, of course, a direct contradiction of Koch's experience, and *may be* true; but it must be remembered that these results were obtained with fluid culture-media; that the difficulty of obtaining pure cultivations in fluid-media is great; and that the method employed (successive cultivation) is one in which the accidental introduction of other organisms renders error easy. In fact, it is far easier to fail than to succeed; so the suspicion arises that the cultivations were never pure or that they became contaminated by other organisms.

2. *That different forms of bacteria are found taking part in the same decomposition* (*e.g.*, putrefaction). This shows simply that several different organisms are capable of living in the same fluid. The process is a complex one, and the products are the result of the life-actions of different forms: it does not show that different forms develop from one species.

3. *That the same form may be found associated with the very different chemical changes.* Thus micrococci, indistinguishable from each other by form or size, occur in relation with pneumonia, erysipelas, small-pox, pyæmia, infective osteomyelitis, and many other diseases. This argument can only be met by tracing the life-history, and examining the products of each organism as described on p. 334.

4. *That the virulence of organisms can be modified in either direction.* Davaine produced an artificial septicæmia by injecting putrid fluids, containing many forms of bacteria, into rabbits, and found that the virulence of the poison increased as the disease was transmitted from animal to animal; but that no increase of virulence occurred after the second or third generation; and Koch showed that this increase was due to the preponderating growth of one of the organisms inoculated and the simultaneous disappearance of all other forms, so that the apparent increase of virulence was really due to the injection of a larger quantity of the specific organisms. Similar increase in physiological activity produced by cultivation has been alleged to occur in other organisms, and has been similarly explained.

Moreover it has already been shown that the virulence of some organisms *can* be modified by cultivation and inoculation.

The whole argument, however, is beside the mark; for variation in intensity of virulence, in whichever direction, accompanied by no morphological or other change, is no evidence against the *individuality* of organisms. As Baumgarten puts it, mitigation of virulence is no better ground for depriving a bacterium of its specific character than

would the extraction of the teeth of a poisonous snake be a reason for regarding it as a non-poisonous species.

5. That one organism can be experimentally converted into another. Buchner stated that by cultivating the non-pathogenic hay-bacillus in meat-infusions, and in unsterilised blood, he made it "wild," and converted it into B. anthracis ; and that by a converse process he converted B. anthracis into B. subtilis. The experiments have been repeated by Koch and others with a negative result. There are distinct morphological differences between the two bacilli, of which Buchner does not seem to have been aware ; and inability to distinguish between the two clearly invalidates the result of the investigation.

This is the experimental evidence as to the **mutability of bacteria**. At present the balance is most decidedly against it, but Koch himself recognises that his experiments do not prove its *impossibility*. Like all other organisms, these unicellular beings must have more or less power of adapting themselves to altered surroundings, and be liable to modification by their environments. They may grow more or less rapidly, may be larger or smaller, and may separate early or remain united in strings, threads, or heaps. On poor substrata the developmental cycle of a polymorphous form may be incomplete, or the cells of a monomorphous form may be stunted and irregular, or abnormal ("involution" Nägeli) forms may appear ; and they may be rendered more or less virulent. But Koch's observations of various bacteria, often extending over years, suffice to show that all he dealt with preserved unaltered, through a long series of cultivations, their inherited characteristics. Whenever the life-history of a species (monomorphous or polymorphous) has been made out, no important departure from its various stages has ever been recorded : the coccus of erysipelas has never been seen to grow into a bacillus or a spirillum.

Looked at from the clinical point of view, every one feels that the best marked group of infective diseases—the specific fevers—must have an unvarying, specific cause. Most observers believe that these diseases never arise except by infection from a previous case. Assuming the virus to be a fungus, they admit that it must at some time have acquired the physiological action which enables it to produce a certain disease ; but they hold that there is no evidence that harmless fungi do at the present time ever acquire such powers. Isolated communities remain free from such diseases for centuries until a case is introduced among them ; then it spreads with the utmost rapidity. In 1520 a negro, covered with small-pox pustules, was landed on the Mexican

coast, where the disease was not then known: three and a half millions are said to have died of it. In 1846, measles was introduced from Copenhagen into the Faroe Islands, and almost every one suffered. Similar facts concerning other acute specifics are given by Sir T. Watson, in the first volume of the *Nineteenth Century*. Murchison and others believed that typhus and typhoid might originate *de novo*, being filth-begotten; but the conditions of life in slave ships and Arctic winter-houses are as insanitary as ever they were in our goals when typhus was endemic in them—yet no typhus occurs. As to the origin of typhoid fever from sewer-gas, many towns and hotels show that exhalations of it may be intense and prolonged without ever generating typhoid fever.

The poison of the most infectious diseases spreads so easily by air, food and clothing, that it is exceedingly difficult to find a case in which the possibility of infection from a previous case cannot be shown. The less infectious kinds have, therefore, been turned to by the advocates of the *de novo* origin. Many cases of diphtheria, believed to have arisen spontaneously, have been recorded; and a urethral discharge like gonorrhœa, in symptoms and communicability, may, it is said, be contracted from a woman suffering from any foul discharge—not gonorrhœal. It is of course quite possible that urethral discharges may be excited by infective irritants other than the gonorrhœal poison. With regard to the so-called "hospital diseases"—pyæmia, septicæmia, and hospital gangrene—there is, perhaps, evidence of some change from non-pathogenic to pathogenic organisms. How otherwise is it to be explained that, when a new building, which has never before contained wounded, is used in time of war as a hospital, these diseases break out as soon as the crowding of the wounded reaches a certain point, whilst they do not attack patients in tents close by? Is it likely that the specific causes were present in the building? Do not the facts tempt to the belief that ordinary bacteria acquire pathogenic properties, or at any rate such a degree of virulence as enables them to become pathogenic by cultivation under the conditions brought about by overcrowding of the wounded? The state of atmosphere produced in the building would seem to be analogous to the "epidemic influence"—that influence which causes infective diseases every now and again to become widely epidemic. From the clinical standpoint, therefore, it would seem that but little evidence is forthcoming in favour of the mutability of bacteria; but the question must be regarded as still *sub judice*

It will be seen that by origin *de novo* is meant—not the spontaneous development of an organism, but the acquisition in an organism of such pathogenic and other properties as may fairly entitle it to be regarded as a distinct species.

VARIETIES AND ÆTIOLOGY OF THE INFECTIVE DISEASES.—The acute specific diseases, to which allusion has so often been made, are now regarded as forming only a class in the much larger group of **Infective Diseases**. An infective disease may be defined as a disease due to the action of a poison or virus which has the power of invading and multiplying in or on living tissues. Infective diseases may be **local** or **general**, just as the effects of organisms may be local or general (p. 322).

There is at present no satisfactory classification of infective diseases. They are generally grouped according to the acuteness of their course, the nature and distribution of their lesions, and such prominent clinical characters as they may possess. The seat of the micro-organisms has been suggested as a basis for classification. Three groups might in this way be made—(1) those due to organisms which do not penetrate beneath the surfaces, but discharge their products into the blood; (2) organisms which thrive in the tissues and produce local effects; (3) organisms which enter the circulation and thrive in the blood (see "Pyæmia and Septicæmia"). In the majority of cases, however, it is still impossible to say into which of these groups a given instance should be placed.

There is, on the strength of the analogy which exists between fermentation and infective diseases (p. 299), a *primâ facie* case in favour of the germ-theory as applied to the infective diseases. And it will be found upon examination of the evidence yielded by actual observation of these diseases, and by experiments upon animals, that the demonstration of the casual relationship of organisms to them is in some cases as complete as it is in the case of fermentation, although in the great majority the proof is still more or less doubtful.

To prove that a micro-organism is the cause of a disease, it is necessary:—

1. That the organism in question, as recognised by its form, mode of growth, or products, be found constantly associated with the disease, at least in its earlier stages; and in sufficient numbers to account for the symptoms.

2. That "pure" cultivations of this organism through several gener-

ations be made, until it may reasonably be supposed that everything, which could possibly have been taken from the animal that yielded the virus, has disappeared.

3. That other susceptible animals be inoculated with the cultivated organism, and that the disease be thus reproduced.

4. That the same organism be found in the tissues of the successfully inoculated animals, in such numbers and with such a distribution as to account for the disease.

The demonstration of a *well-characterised* organism in *constant* association with a disease is now by many taken as almost equivalent to proof that it is the cause of the morbid process. For it is, in most cases, impossible to experiment on man, and frequently no animal can be found which suffers from the disease under investigation. Consequently, the proof cannot be carried beyond the first stage. This, however, is no proof at all to those who believe that under certain circumstances a certain form of organism will develop spontaneously; nor is it satisfactory to others who think that, when a nidus favourable to a certain organism exists, that organism is sure to drop into it. Sidney Martin has suggested that an attempt should be made to discover and separate the chemical products of the organism, both in the tissues of the animal or person dead of the disease, and in the subsequent culture-ground. If suitable media are selected, these products should clearly be identical.

The amount of patience and skill necessary to carry on an investigation of the above kind can be appreciated only by those who have worked at the subject. *They* are not surprised that so few diseases have been thoroughly investigated. In the case of man, the difficulty of obtaining material in the early stages of diseases, and immediately after death, must also be taken into account. Until quite recently, too, the methods employed were wholly inadequate to the discovery of many kinds of fungi. At first there was unaided microscopic examination only, and with inferior objectives. The detection of all fungi, under these circumstances, was very difficult, and often impossible. A considerable step was made when von Recklinghausen, in 1871, pointed out that the uniform size of micrococci and their resisting power against dilute acids and alkalies and glycerine, might be employed as a means of diagnosis between them and fatty and albuminoid particles. But progress has been much more rapid since the introduction by Abbe of a powerful sub-stage condenser, by Weigert of the aniline dyes as stains for organisms, and by Koch

of many improvements in the mode of examining specimens and of carrying on pure cultivations.

IMMUNITY FROM INFECTIVE DISEASES. — Some diseases tend to recur again and again in the same individual. Of these, bronchitis and facial erysipelas are prominent examples. Other diseases show a precisely opposite tendency. To have suffered once from one of them is to have secured almost certain freedom from a second invasion. Freedom thus ensured is known as *acquired immunity.* Persons, for example, who have had small-pox are said to be immune against a second attack. The same is practically true of typhoid fever, measles, and other specific diseases. It is by no means certain how long such immunity lasts; and, in man, there are no means of definitely ascertaining its duration. Again, certain diseases which are common in some species of animals are practically unknown in others very closely allied to them. Thus tubercle is common in pigs and cows, but excessively rare in sheep, goats, horses, and asses. Mice fall a ready prey to anthrax, while rats escape unharmed. Accordingly, pigs and cows are said to be *susceptible* to tubercle; while sheep, goats, horses and asses are in like manner said to be *immune* against it. The exact conditions on which this susceptibility or immunity depend are unknown. To distinguish it from the acquired form, it is known as *natural* or *inherited immunity.* When an animal is only slightly susceptible, and yet not absolutely immune, it is often termed *refractory.*

In human pathology there are also many examples of these peculiarities. Negroes are immune against yellow fever: white races are susceptible. A nurse in a fever hospital may never have had scarlet fever, and yet may continue to resist all exposure to the infection. It may be that inherited immunity is due to the handing down to offspring of that acquired by ancestors. Thus races, among which certain acute fevers (like measles) are common, suffer much less severely than those among whom the disease appears only at very long intervals. The complete immunity of the negro to yellow fever is generally accounted for by supposing that those who could resist the disease best would, by living longest and having most children, be most likely to hand on their peculiarities to the succeeding generation: and further, that the degree of immunity thus gained would be strengthened by the intermarriage of those already partly immune. But this explanation offers no adequate reason for the peculiar sporadic

immunity enjoyed by some individuals, as in the case of the fever-nurse just cited. Occasionally this sort of immunity is more apparent than real. Two medical students paid almost daily visits to scarlet fever wards for several months, and failed to contract the disease; but late one afternoon, on entering the wards much exhausted by severe exercise and a fast of five hours, both took the disease in a severe form, and one died.

Artificially Acquired Immunity.—Three forms of preventive inoculation have been employed to secure immunity from disease, or to arrest the development of contagia that have already reached the tissues.

1. Inoculation with the attenuated virus of the original disease.

2. Inoculation with the chemical products of the organisms of the original disease.

3. Inoculation with serum obtained from an animal that has been treated by one of the two preceding methods.

1. It has been well known since the sixth century that the artificial inoculation of small-pox produces, on the one hand, a mild form of the disease, and, on the other, confers upon its subject immunity against a second attack. In one country after another it has for a time been the custom to practise inoculation to ensure this result. It has also long been recognised that epidemics vary in severity, and that mild attacks and severe attacks are equally efficacious in securing immunity.

Pasteur was the first to place preventive inoculation on a scientific basis. He demonstrated that the virulence of some contagia can be varied by experimental procedures. In the case of chicken-cholera, he showed that by exposing cultures of the virus for long periods its virulence became so reduced that inoculation of the weakened or *attenuated* organisms gave rise to a comparatively mild disorder, which, however, sufficed to secure immunity against subsequent attacks. Other observers have since shown that the virulence of many other organisms can also be modified, and that the organisms can be kept in their attenuated condition through several cultivations; though there seems to be a general tendency for them to return to their previous degree of virulence. The attenuation is generally effected by one of two methods.

(1) A series of animals is experimentally selected, generally on account of their slight susceptibility to the disease in question. Successive inoculations are then made from one to another, until it

is found that the desired degree of attenuation has been reached. (2) Cultures of ordinary virulence are exposed to the air, or to an increased temperature only slightly below the fatal limit, or to the action of small doses of various antiseptics. Pasteur's treatment of persons bitten by rabid animals is the best known illustration of this method, though no hydrophobia-organism has yet been discovered. By a series of successive inoculations, a special virus is prepared which is known to have—when injected into rabbits—a constant incubation period of six days. Rabbits are inoculated with this virus, and their spinal cords are subsequently dried very gradually in the presence of caustic potash. The longer the drying is continued, the weaker the virus becomes. If an emulsion of a cord, that has been dried for six days, be made, and inoculated upon rabbits, it entirely fails to produce the disease. Pasteur's method is to give ten injections, extending over four days, according to the following table :—

First injection,	1st day,	Emulsion of cord dried			ten	days.
Second ,,	1st ,,	,,	,,	,,	nine	,,
Third ,,	1st ,,	,,	,,	,,	eight	,,
Fourth ,,	2nd ,,	,,	,,	,,	seven	,,
Fifth ,,	2nd ,,	,,	,,	,,	six	,,
Sixth ,,	2nd ,,	,,	,,	,,	five	,,
Seventh ,,	3rd ,,	,,	,,	,,	four	,,
Eighth ,,	3rd ,,	,,	,,	,,	three	,,
Ninth ,,	3rd ,,	,,	,,	,,	two	,,
Tenth ,,	4th ,,	,,	,,	,,	one	day.

After three days a few more injections are given daily, and the process is complete. Statistics are strongly in favour of the efficacy of the method. There is generally plenty of time to carry it out, as the incubation-period in man is never less than twelve days and usually about six weeks.

This method of securing immunity is not applicable to the vast majority of specific diseases. On the one hand, certain organisms, such as the tubercle bacillus, have hitherto defied all efforts made to attenuate them, and, on the other, there is some risk, even after attenuation, that the disease may be produced in a virulent form.

2. To avoid this latter danger the chemical products have been freed from the living organisms and injected alone. The organisms can be removed by filtering fluid cultures through porcelain ; or they

may be killed by the action of heat, or of some volatile antiseptic, such as oil of mustard, which can be subsequently removed. Sometimes the full degree of immunity attainable is reached after two or three injections, but in other diseases and other animals the injections have to be repeated every two or three days for several weeks or even months. Immunity thus conferred is not always very certain, nor of long duration; and the method is not attended with favourable results in those cases in which exposure to infection precedes its application.

Haffkine's vaccination against cholera illustrates both this and the preceding method. He employs two vaccines. One is made from an attenuated virus, the other from an exalted virus. The attenuated virus is prepared by cultivating the cholera-spirilla in aërated media at a temperature of 39° C. (102·2° F.). The exalted virus is prepared in the following manner. A pure culture of the organism is introduced into the peritoneal cavity of a guinea-pig. Death follows in twenty-four hours. The peritoneal fluid is immediately removed and another guinea-pig similarly inoculated. This process is continued through a series of animals until the interval between inoculation and death falls to its lowest limit. Persons to be protected are vaccinated twice. On the first occasion, the attenuated virus is used; on the second, three to five days afterwards, the exalted virus. The vaccination is supposed to produce a sufficient tolerance to the cholera-poison to enable the body to "react" more vigorously when attacked in the ordinary way. Sometimes the *living* cultures are used, but more often the vaccine is *sterilised* by the addition of carbolic acid. Prepared thus the fluid can be more easily preserved, and can be introduced with less risk; but, as in other cases, the results are neither so certain nor so prolonged. The sterilised products of bacteria, irrespective of their exact nature, are often termed *toxines*.

3. These results led Behring in 1890 to examine the *serum* of animals thus immunised, and since that time many observers have followed in his footsteps. In the case of tetanus, the serum of immunised rabbits was used, and three very remarkable results were established. It was found that—

(1) Repeated injections of this serum will render mice, which are particularly susceptible to the disease, absolutely immune.

(2) The addition of the serum to living or to sterilised cultures of the bacillus will completely destroy the pathogenic power of each.

(3) The injection of the serum into animals already suffering from tetanus will not infrequently lead to absolute recovery.

Furthermore it was found that while the ordinary serum of a naturally immune animal possessed none of these properties, they could be developed by a series of similar inoculations.

This method, when applied to the treatment of disease already contracted, is known as *serum-therapeutics,* or treatment by *anti-toxin.* It has been employed in tetanus, with not very satisfactory results, but is more extensively used * in diphtheria. The various stages, comprising the whole process as given by Roux at the Budapest Congress in 1894, will serve as an admirable illustration. They are as follows :—

(1) A pure culture of the bacillus diphtheriæ (Lœffler) is made. This takes about three weeks.

(2) The organisms are removed by filtration through porcelain.

(3) The toxine thus obtained is injected into the horse in small quantities, two or three times a week, until no reaction follows. This period extends over from one to three months.

(4) Some of the blood is then withdrawn, and the serum is separated, sterilised, and stored for subsequent use.

(5) When required for the treatment of diphtheria, a dose of about 20 c.c. is injected under the skin. A second dose is occasionally required. Improvement follows in the course of twenty-four hours.

The active principle contained in the serum is unknown. In this country it is generally referred to as "anti-toxin."

Attempts have been made to deal with tuberculous disease in the same manner. The tubercle bacillus has, however, successfully resisted all attempts made to attenuate it; and to inject the organism in its ordinary degree of virulence, is simply to inoculate the disease from which immunity or relief is sought. The next step was made by Koch, who prepared a sterilised extract of its products, which was known as "tuberculin." This, when injected, produces an inflammatory reaction at the sites of tuberculous infection. At the present time, experiments are being made to discover an anti-toxin, analogous to that just described in connection with diphtheria.

It may here be mentioned that ordinary healthy blood-serum is found experimentally to be in many cases a distinct germicide. If anthrax organisms be suspended in it most of them will die. Evidence has

* November, 1894.

been adduced to show that this germicidal action is due, at any rate in part, to the action of nuclein. It was found that digestion of the serum did not remove this influence, but that a temperature of 55° C. (131° F.) did. It was accordingly assumed that, while the action was clearly not due to albumin, it was still most likely due to some form of proteid. The proteids were therefore precipitated with alcohol and ether, and the precipitate digested with pepsin and hydrochloric acid. The undigested residue was then washed and sterilised. The compound thus obtained gave the reactions of nuclein, and was found to possess a germicidal power over cholera-spirilla, staphylococcus pyogenes aureus, and asporogene anthrax.

Theories of Immunity.—Much controversy has taken place during the last few years concerning the real nature of the immunity which has been discussed in the preceding pages.

It is well known that immunity against some chemical substances can be obtained by certain persons. Opium-eating and arsenic-eating are illustrations of this. Furthermore, it has lately been shown that if minute but gradually increasing doses of ricin—the active principle of the castor-oil bean—be given by the mouth to guinea-pigs, they can be rendered so far immune against the action of the poison, when injected subcutaneously, that they will survive a dose four hundred times that ordinarily sufficient to produce death. In other words, the tissues of the higher organisms possess a certain power of adapting themselves to a new environment if only a sufficient time be allowed. But as soon as we attempt a detailed explanation of these results, as well as of those previously mentioned, we find that they appear in many cases to be absolutely contradictory. The serum of some immune animals is fatal to cultures of the virus in question ; in other cases it is not. Again, while the serum may be fatal to cultures, the blood itself may have little or no resisting power against the organisms when introduced into the body. Possibly the term "immunity" covers several dissimilar and complex processes. It is sufficient to mention that there are two views current. According to one, immunity is simply a question of chemical reactions ; according to the other, it is due to vital forces which are called forth by the action of the virus. Metchnikoff, in his "phagocytosis" theory, considers that it depends mainly upon the specific action of certain of the leucocytes (p. 297).

Pathogenic Bacteria.

A more detailed reference must now be made to certain micro-organisms, which, on more or less satisfactory evidence, are believed to be the exciting causes of certain infective diseases. For want of a better classification we shall follow Cohn's (p. 335).

I. **SPHÆROBACTERIA or MICROCOCCI.**—These are round or oval cells, generally ·5 μ to 2 μ in diameter. They are

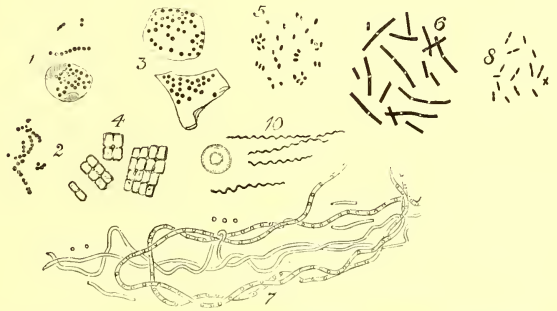


FIG. 121. — 1. Micrococci from an acute abscess—streptococci free, staphylococci in a pus-cell. 2. Streptococci from secondary suppuration in the elbow, occurring in puerperal fever. (Horsley.) 3. Micrococci in cells from gonorrhœal pus. 4. Sarcinæ ventriculi. 5. So-called bacterium termo. 6. Bacilli anthracis, from blood of mouse. (Horsley.) 7. Chains from cultivation of B. anthracis; some bearing spores. (After Duclaux.) 8. Bacilli of typhoid fever, from a mesenteric gland. (Gibbes.) 10. Spirilla of relapsing fever, and red corpuscle. (After Vandyke Carter.) × 500.

arranged singly; in pairs (*diplococci*); in chains (*streptococci*) of four cocci to three hundred, which may be straight or wavy; in groups like bunches of grapes (*staphylococci*); or in colonies and zooglœa-masses. The organisms belonging to this order differ among themselves in form, size, mode of grouping, and physiological action.

The absence of distinctive form makes it very difficult to ascertain whether a culture is "pure," and whether a coccus under observation is the cause of a disease in question. Of all forms of fungus, cocci are the most frequently associated with disease.

1. **Fermentation of Urine.**—The *Micrococcus ureæ* is one of the causes of the ammoniacal fermentation of urine, which it enters from the air. Urine obtained pure, and exposed only to pure air will keep

acid for years. The transformation of urea into ammonium carbonate is said to be usually due to the action of an "unformed" ferment secreted by this micrococcus. The ferment, however, must be indiffusible, for the urine in an excised bladder does not putrefy even if placed in putrid urine. The change often occurs in urine contained in the living bladder, and may extend up to the pelvis of the kidneys with the most fatal results (see "Suppurative Nephritis"). The M. ureæ is rather large (2 μ) and occurs singly or in chains.

Leube has demonstrated the existence of four other distinct bacteria producing the same effect on urea. These and the M. ureæ are capably anaërobic, and may therefore be the causes of putrefaction of



FIG. 122.—*Staphylococcus Pyogenes Aureus.* From a culture.

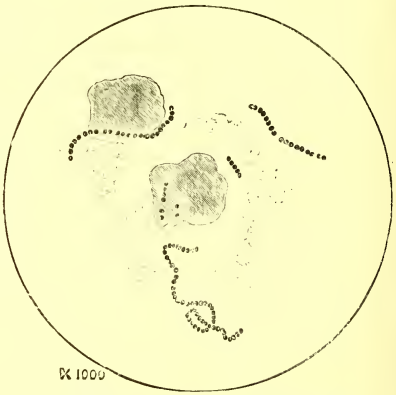


FIG. 123.—*Streptococcus Pyogenes.* From pus found in a pyæmic abscess.

urine in the bladder. Miquel has discovered a delicate bacillus, which has a similar action, and is anaërobic

2. **Suppuration**, or **pyosis**, whether in the form of acute abscess, osteomyelitis, or metastatic pyæmia, is usually associated with the presence of cocci. Many varieties of cocci are described as occasionally present. By far the most common of these are the *Staphylococcus pyogenes aureus*, the *Staphylococcus pyogenes albus*, and the *Streptococcus pyogenes*. They all grow readily at the body temperature. The *Staphylococcus pyogenes aureus*, and the *staphylococcus pyogenes albus* differ from one another in only one important particular; namely, that the former, when cultivated on gelatine, agar-agar, or potato, in the presence of oxygen, produces a pale orange pigment, while the latter

does not (see Frontispiece). They resemble one another in forming clusters, in liquefying gelatine, and in being able to exist for weeks in the dry state. Moreover, when introduced into the tissues under favourable circumstances they both form a peptonising ferment; albumoses and peptones can always be obtained from pus. The *Streptococcus pyogenes* consists of cocci rather larger than the preceding, and grows in chains. It does not liquefy gelatine, and does not form pigment. When introduced into the tissues it peptonises even more vigorously than the staphylococcus. The staphylococcus is principally found in circumscribed abscesses; while the streptococcus is especially associated with spreading and diffuse suppuration.

All these organisms exist in considerable numbers on the skin, especially where they can "obtain cover." They reach wounds by growing under the dressings, and not, as a rule, by falling from the air. Minute quantities of boric acid (1 : 300, applied to cultures) and other antiseptics suffice *to stop their growth*. Observers are by no means agreed as to the length of time which a 1 : 1000 solution of mercuric chloride takes to *kill* them, the times given varying from eight seconds to thirty minutes. Possibly some of this difference depends on the different virulence of the specimens tested, and may be said to be consistent with the results obtained by inoculation.

In the case of these organisms the chain of proof demanded (p. 339) is complete. Ogston inoculated eggs with cocci from an acute abscess. By a series of cultivations he obtained the cocci "pure," and with these he successfully inoculated animals. Although abscesses were the usual results, well-marked septicæmia occurred in some cases. Cocci were then found in the blood, though never in very large numbers.

Further proof that these organisms can cause suppuration has been given. Similar operations were performed with antiseptic precautions on both eyes of each of a series of rabbits, and one eye in each animal was inoculated with pyogenic cocci, chiefly the staphylococcus p. aureus: all the aseptic eyes healed without suppuration, while all those infected suppurated and were destroyed, except some in which the operation was quite superficial (Knapp). Upon man numerous experiments have been made: cultivations of staphylococci have been inoculated upon the cutis and have led to the formation of small abscesses. Similar cultivations have been rubbed into the normal skin of the arm and have induced the formation of numerous impetiginous pustules. Boils, and, in one case, a large carbuncle, have been produced

in a similar manner. Lastly, the subcutaneous injection of these organisms has resulted in the formation of abscesses (p. 324).

Under ordinary circumstances pyogenic cocci can enter the skin by the orifices of ducts or through small abrasions. Impetigo results if they gain entrance to the ducts and multiply there without penetrating the true skin. If the cocci reach the depths of a hair-follicle or sweat-gland their action is more violent, and they produce a slough—a boil results. When the cocci actually penetrate the cutis vera they cause an abscess of the skin.

In **metastatic pyæmia** the proof is not quite so complete. Large numbers of micrococci are found in the secondary foci. It has, moreover, been shown that the unhealthiness of the wound is in proportion to the number of zoogloœa-masses on its surface, and the severity of the disease to the number of cocci in the blood; whilst the cocci have been traced from the wound into connective-tissue interspaces and even into a vein. They are present in all clots undergoing infective softening. On the other hand, large numbers of cocci have been found in the blood of healthy persons.

Concerning the special organism present, it may be noted that Rosenbach examined six cases of metastatic pyæmia and found the *streptococcus pyogenes* in five, in two of which it was accompanied by a smaller number of the *staphylococcus pyogenes aureus*. In one case—the only one which recovered—the latter coccus occurred alone.

In **acute osteomyelitis**, Rosenbach demonstrated that the *staphylococcus p. aureus* was present in the great majority of cases; and he was further able to support Lœffler in his statement that the same organism, when injected into the veins of animals whose bones had been bruised or fractured, caused acute osteomyelitis—and this whether the source of the organism employed was a case of osteomyelitis or a boil.

Spreading traumatic gangrene often seems to be due to the *streptococcus pyogenes*. Ogston found that injections of *staphylococci* might cause similar gangrene of the skin in animals. Koch induced a spreading gangrene in rabbits by injections of a little putrid blood, and in his cases only *streptococci* developed. In two cases of spreading traumatic gangrene, in which subcutaneous emphysema was a marked feature, Rosenbach found a *bacillus*, very few cocci being present.

Lastly, the above cocci may give rise to *inflammation stopping short of suppuration*, the streptococcus being associated with the *more diffuse* varieties. Cocci are frequently associated with inflammations about

the fauces, even without the presence of pus. The evidence we have of the infective nature of papillary and ulcerative endocarditis is given in Chapter xxvi.

In the large majority of cases in which pyogenic cocci are introduced into the tissues only local results follow. In the presence of conditions favourable to the growth of the organisms they tend to spread. With especial ease they are carried to the lymphatic glands. There they become arrested and give rise to glandular abscesses. Thence, once more, their progeny and their products are distributed to more distant parts—it may be throughout the body. Shattock has drawn a parallel between this process and that which follows "tubercular" infection. As the latter is called "tuberculosis," he suggests that the process we are now considering should be named "pyosis."

The circumstances under which these very different results follow are unknown. The probable factors have been already discussed (p. 321).

Erysipelas.—Micrococci have often been described in erysipelatous skin, especially at the spreading edge. They occupy the lymphatic channels and spread along them: hence the name—infective capillary lymphangitis. Orth produced typical erysipelas in a rabbit by subcutaneous injection of the fluid from an erysipelatous bulla; with œdema-fluid from this animal he successfully inoculated a second: the fluid and affected skin contained cocci in large numbers. He next cultivated the fungus, and produced erysipelas by injecting it. In 1881 Fehleisen found chains of cocci constantly present in pieces of skin excised from the *spreading edge* of an erysipelas rash. The cocci filled the *lymphatics* of the *superficial part* of the corium, like an injection-mass, and occasionally extended to the subcutaneous fatty tissue, but were *never* found in the blood-vessels. Round-celled infiltration and dilated blood-vessels marked their presence; and in parts where the inflammatory zone had disappeared, the cocci had vanished also. The organisms were cultivated upon gelatine through fourteen generations in two months: eight out of nine rabbits, subsequently inoculated, suffered from the disease; and six out of seven inoculations upon man were equally successful. The incubation was fifteen to sixty hours; then followed rigors, fever, and typical rash. The evidence assigning a causal relationship to the streptococcus is therefore complete. Immunity, if conferred at all, did not last two months. Three per cent. solution of carbolic acid, or one per thousand of mercuric chloride, sufficed to destroy the vitality of the fungus.

Fehleisen stated that the *streptococcus erysipelatis* presented distinct, though slight, differences from the streptococcus pyogenes, and that it never caused suppuration; if abscess occurred with erysipelas it was due to a mixed infection. The majority of recent writers upon the question have failed to detect either morphological or physiological differences; and many are therefore inclined to think that the two organisms are identical, and that the point of inoculation, attenuation of the virus, and similar conditions, must determine whether erysipelas or diffuse subcutaneous suppuration shall occur in any given case. The clinical differences between the two diseases would seem to warrant hesitation in accepting this view until it has been proved that the streptococcus erysipelatis, taken from a case of undoubted erysipelas, can cause diffuse suppuration, and, on the other hand, that the streptococcus pyogenes from an acute abscess can give rise to erysipelas. No case of erysipelas, from inoculation of a wound with pus containing streptococci, seems to have been recorded.

Gonorrhœa.—Neisser, in 1878, discovered in the urethral pus a large micrococcus (*gonococcus*, Fig. 124), peculiar to this disease. He recognised it by "facets" or flattenings on the surfaces in contact, such as are now known to occur in other rapidly multiplying cocci. It is distinguished from ordinary cocci by its size; by the constant interval, about equal to the diameter of the coccus, between the individuals in the groups; and by the frequency of its occurrence *upon* and *in* the pus-cells. Neisser considered its presence a means of diagnosing gonorrhœal from other discharges. It was subsequently shown that the separation of the cocci is due to swelling of their capsules. It multiplies by fission in two planes alternately. In the first stage it is a diplococcus, each coccus having a bean-shaped outline. In the next stage each "bean" subdivides, and a tetracoccus is formed. The number of cells affected is always relatively small, and varies in different cases. The coccus is cultivated with much difficulty. Cultures were first carried out successfully by Bockhardt. This investigator injected a "fourth" cultivation into the urethra of a general paralytic, and produced a purulent discharge. The man died of pneumonia ten days later, and an examination of the urethra led Bockhardt to believe that the cocci probably pass through the epithelium into the lymphatics of the fossa navicularis, where they excite acute inflammation. They enter into white corpuscles, and either pass with them into blood-vessels, where they die, or they come away in the pus.

Since then Bumm has succeeded in cultivating the gonococcus upon solidified blood-serum; he inoculated a second and a twentieth culture upon the female urethra, causing typical gonorrhœa in each of the two cases. The proof of causation, thus placed beyond doubt, was difficult to obtain, as no animal is susceptible to the disease.

With regard to complications—the occurrence of suppurative lymph-adenitis (bubo), which is unusual in gonorrhœa, is said to be due to infection of the gland by ordinary pyogenic organisms, the urethra in these cases being the seat of a mixed infection. The gonococcus,

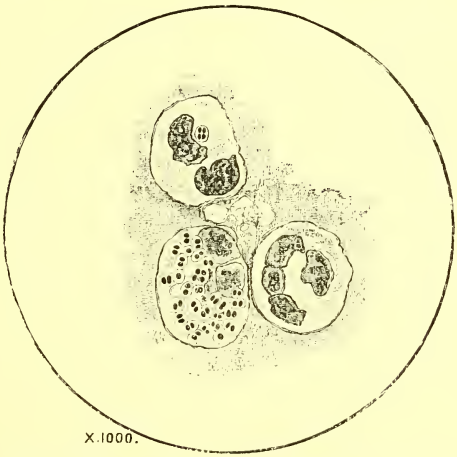


FIG. 124.—*Gonococci from Urethral Pus.* The cocci are *in* the pus-cells. There are two tetrads and two single cocci, the rest are diplococci. The three cells shown are all of the multinucleated variety.

injected into subcutaneous tissue, does not cause suppuration, but disappears in twenty-four to thirty-six hours.

The evidence as to the presence of the gonococcus in joints, which are the seats of gonorrhœal arthritis, is contradictory: perhaps arthritis, also, is the result of a mixed infection, but we may note that it is quite unusual for gonorrhœal joints to suppurate.

The gonococcus is incapable of multiplying external to the body, except under the very special conditions of a culture. Its resisting power is feeble and it soon perishes. If this were not so, considering the great frequency of the disease, infection otherwise than by contact would almost certainly occur.

Pneumonia (see Chapter xxxi.).—The production of acute pneu-

monia has been attributed to two distinct organisms. (1) The first, known as Friedländer's pneumococcus, though, strictly speaking, it is a *microbacterium*, was discovered by that observer in 1882. He found great numbers of these organisms in the early stages of pneumonia, not only in the exudation, but also in the lymphatics of the lung and in the fluid of any pleurisy or pericarditis which was present. These cocci are oval or rod-shaped; they are contained in oval or elliptical capsules with rounded ends. Two, four, or even more, cocci may be found in these capsules. The capsule is dissolved by alkalies and by water; is contracted by acetic acid (like mucin); is present only in the lung; is scarcely or not at all developed in cultures; and is best stained in cover-glass preparations by immersion for two to three minutes in a solution of gentian violet in aniline water, followed by treatment with alcohol for half a minute.

Friedländer subsequently stated that he had cultivated the coccus in blood-serum and gelatinised meat-infusion and on potato. Introduced by needle-puncture into the two former substrata, the growth takes the very characteristic form of a round-headed nail; on the latter ground it forms greyish drops. Diffused in distilled water and injected into the lung and pleura of rabbits, the organisms produced no effects; but of thirty-two mice inoculated, all died in less than twenty-four hours. The lungs were very red and almost universally solid, and the spleen was enlarged; both organs contained the characteristic cocci, which were also present in considerable numbers in the blood, and in enormous numbers in some fluid which occupied the pleura. Guinea-pigs were more refractory to the poison, and, out of five dogs, only one suffered.

Baumgarten is strongly of opinion that this parasite has no pneumonia-exciting action in man, but that it enters the pneumonic patch from the upper air-tubes or pharynx, and multiplies in the inflamed tissue. For it seems that apparently identical "capsule cocci" are not uncommonly to be met with in pus, in the epithelium of the mouth, in sputum, or in the secretion of nasal catarrh in otherwise healthy men. A still more serious objection lies in the fact that other observers have not been able to demonstrate this organism with the constancy of which Friedländer spoke. The *strongest* objection, however, seems to be that the cocci found and the cocci cultivated are not identical; for Friedländer considered that his coccus retained the aniline stain when treated with Gram's iodine solution, whereas the coccus which he cultivated is decolorised by this treatment. The cocci, which remained stained in sections of pneumonic lung pre-

pared according to Gram's method, were therefore not the cocci Friedländer cultivated, but were probably those subsequently demonstrated by A. Fränkel and Weichselbaum, to the description of which we now pass.

(2) Fränkel and Weichselbaum independently demonstrated the presence in pneumonic lungs of another organism—the **pneumococcus** or **diplococcus pneumoniæ**. This consists in cultures of round or oval cells, usually in pairs, but often in chains of four to ten or even twenty to thirty. These longer chains are much straighter than those of ordinary streptococci (Weichselbaum). In the tissues, the microbes often become lancet-shaped, and their pointed ends may be towards or away from each other, usually the latter. These cocci have capsules just like Friedländer's, and they may be similarly stained. *They retain the aniline stain when treated by Gram's method.* Kruse and Pansini insist on the variability of form. They describe no less than thirty varieties.



FIG. 125. — *Diplococci Pneumoniæ* entangled in the meshes of the fibrinous exudation. From a section of lung in the red hepatisation stage of acute pneumonia. In the upper part of the field is a cell containing several cocci—possibly a phagocyte. × 1000.

Whereas Friedländer's coccus can be readily cultivated on gelatine at 70° F., Fränkel's is best grown on agar at a temperature of 95° F. to 98·5° F.; and the growth is scanty and not nail-shaped, but of characteristic "dew-drop" form. When the organism is grown on gelatine this medium is not liquefied. In many of its characters it thus resembles the streptococcus pyogenes. The substratum must be kept slightly alkaline or growth ceases. Even when transferred daily from tube to tube the diplococcus rapidly loses its virulence and assumes the streptococcus form: to preserve or to restore its pathogenic power, an occasional inoculation upon a susceptible animal must be resorted to. Cultivation for one to two days at 107° F. destroys the virulence; it is weakened by longer culture at slightly lower temperatures.

Subcutaneous injections of virus of *full intensity* into rabbits, mice, and guinea-pigs cause an acute, generally fatal, illness, like septicæmia, with characteristic post-mortem appearances; but there is no sign of

pneumonia. An *attenuated* culture introduced beneath the skin does sometimes give rise to pleurisy or pneumonia, or both; and these results are usual after *injection* of such a culture *into the lungs*. Then the appearances usually very closely resemble those in pneumonia and pleurisy in man, and the exudation contains large numbers of encapsuled cocci. Pericarditis also may ensue.

The inoculation either of filtered cultures of the organism, or of the serum of animals vaccinated with them, is, in each case, said to confer a temporary immunity. Issaeff asserts that the cocci thrive in cultures treated with the "immunised serum"—a result altogether contrary to that obtained under similar conditions in tetanus (p. 344). Sputum *before* the "crisis" is virulent; but sputum *after* the "crisis" is said to confer immunity.

Baumgarten believes that this coccus may be regarded as *constantly* present, for, though Weichselbaum found it in only ninety-two per cent. of a large number of cases, his method of examination rendered it possible to miss the coccus; and if it really was absent in any cases, it might have been dead at the time the cases were examined; for, as in cultures, so probably in the body, the diplococcus pneumoniæ has but a short life. These cocci occur in sufficient numbers to account for the symptoms.

Besides being present in pneumonic lung, it is occasionally found in the blood (sparingly) and spleen, and in inflammations arising independently, or during the course of, pneumonia—pleurisy, empyema, meningitis, endocarditis, peritonitis, and otitis media. But it appears to be an *occasional* denizen of the mouth, also occurring in the saliva and in the middle ear of healthy people. This suggests that it is only an accidental parasite in pneumonia. Against this view the following points seem to tell: its inconstancy in the mouth; its constant occurrence in pneumonic lung, sometimes as the *sole demonstrable organism;* its distribution, not uniform in the inflamed area, but chiefly at the spreading edge and in the surrounding œdema. Pneumonia does not follow inoculation unless the parasite is localised in the lung. Salvioli says that he succeeded in inducing lobar pneumonia in guinea-pigs by intra-tracheal injection of pneumonic exudation containing these cocci; but Fatichi failed with rabbits. Further experiments of this kind are required, for there is every reason to believe that in man infection occurs through the lung, though in some cases the disease in this organ may be secondary, or at any rate merely one of several morbid changes.

When pneumonia runs on to suppuration and gangrene, these complications are possibly due to a secondary infection by the staphylococcus pyogenes aureus or streptococcus pyogenes; though pyogenic effects have been attributed to the unaided pneumococcus.

Micrococci have been described in *Measles, Vaccinia, Variola,* epidemic *Cerebro-spinal Meningitis, Typhus Fever, Acute Yellow Atrophy of the Liver* (early stage), *Whooping-cough, Dysentery, Fat Necrosis,* and many other diseases, but the evidence in favour of their causal relationship to the respective diseases is not sufficient to justify a description of them here.

A micrococcus which divides in three diameters, at right angles to each other—**Sarcina**—is often found in vomit from stomachs dilated from pyloric obstruction and in cases of dyspepsia from chronic catarrh (*Sarcina ventriculi*); in the bronchi and deeper parts of the lungs in phthisis (*Sarcina pulmonum*) and in the urine (*Sarcina urinæ*): it has been seen also in abscesses and in blood. Single cocci may be seen, but the majority form cubical groups of four, or some multiple of four (Fig. 121). S. ventriculi (2·5 μ) is larger than S. urinæ, or than the fungus of this shape occurring in the lungs (1 μ to 1·5 μ). Sarcinæ may occur in the stomach without appearing in the urine or elsewhere. It is extremely difficult to get rid of the fungus when it is once established. The nature of the decomposition to which it gives rise is unknown.

MICROBACTERIA.—This group contains no organism pathogenic in man.

DESMOBACTERIA.—The members of this group are slender rods, of which the length is generally much more than twice the breadth. They multiply by transverse division, and often grow into long, jointed, but unbranched filaments, without constrictions at the joints. Formation of spores has been detected in some species. All the pathogenic organisms in this group are straight: they are known as **bacilli**.

The **Bacilli** of **Tubercle, Leprosy, Syphilis, Glanders,** and **Rhinoscleroma** are described in the chapter on the "Infective Granulomata."

Splenic Fever.—The *B. anthracis,* found in this disease, is the best known of all the parasitic fungi. Its life-history was worked out by Koch. In blood from the spleen of animals, dead of splenic fever,

are found enormous numbers of rods, 5–20 μ long by about 1 μ broad. They have slightly concave ends, are straight and motionless (Fig. 121, p. 347). In a suitable culture-material, such as the blood of the dead animal, with a plentiful supply of oxygen, and a temperature between 60° and 107° F. (77° to 87° F. being most favourable), the rods grow into very long interlacing filaments often grouped into convoluted bundles (see Frontispiece). In these filaments, round, highly refracting spores form at short and regular distances; the bacilli now break up, and the spores are set free. Under favourable circumstances these grow into bacilli. In living animals, long filaments and spores are never found, the rods multiplying solely by division. The rods exist in enormous numbers in the capillaries, especially those of the spleen, lungs, liver, kidneys, and mucous membrane of the intestine (Fig. 117, p. 323). Numbers leave the body in the urine, fæces, and blood flowing from the nose and mouth of the animal before it dies; thus the ground in its neighbourhood is covered with the fungi. In bodies buried at the depth of one metre, where there is neither oxygen nor a suitable temperature, no development of spores occurs, and the bacilli soon die. As to the mode of infection—Pasteur says that the mouths of animals are wounded by siliceous grasses, and believes that the cuts thus made are inoculated with bacilli or spores. This view is supported by the frequent swelling of the cervical glands in sheep; but both these animals and man are frequently infected by insects which bite them on the face. Koch thinks the intestine is the commonest seat of infection. Klein, however, records a case in which one mouse ate most of another that had died of splenic fever, without any ill results. In warm, marshy districts the bacilli form spores plentifully; these are carried by floods to meadows where anthrax may not have previously occurred.

In man, malignant pustule is due to inoculation with the B. anthracis; and generally, in this country, from wool or hides brought from countries where the disease in endemic. Some time after the appearance of the pustule, general symptoms appear, bronchitis or diarrhœa being common. Davies-Colley found numerous bacilli in serum pressed from an excised pustule, and in the sputum, urine, fæces, and sweat. The patient recovered; but though free from symptoms, he was still eliminating in his urine a few bacilli a month after excision of the pustule. In some cases there is no superficial lesion, and the symptoms may be those of acute septic poisoning, or be chiefly pulmonary or intestinal (Woolsorter's Disease). Perhaps the

predominant symptoms indicate the mucous membrane through which infection has taken place (p. 316). The products of the anthrax bacillus are shown in the table on p. 321. Other facts regarding the B. anthracis are given in the earlier part of the present chapter.

B. anthracis is constantly present in splenic fever, and ultimately in enormous numbers. The blood of a fœtus, in an animal with splenic fever, contains no organisms, and does not produce the disease; whilst blood, containing spores or bacilli capable of development, always does so in suitable animals. The bacilli may be separated by filtration, washed with distilled water, alcohol, ether, and then dried; but, notwithstanding all this, they can still cause splenic fever. Pure cultivations may be made through fifty generations, with the same result. They never give rise to any other disease. If this is not proof that B. anthracis is the *cause* of splenic fever, the belief that *itch* is due to the acarus scabiei, or that trichinosis is due to trichinæ, must also be regarded as ill-founded.

By cultivating B. anthracis for twenty days at 107° to 109° F., and using the vaccine for repeated inoculations upon sheep and cattle, Pasteur rendered these immune to the spontaneous disease and to the action of the virulent virus. After much controversy, the possibility of this "attenuation" has been fully established; there is, however, still some doubt as to the value of vaccination against splenic fever; Koch, for instance, maintaining that to be of any use, the vaccine must be so strong that some animals, and perhaps very many, will die of the disease induced. The attenuation of anthrax bacilli has been brought about in other ways—by cultivation in air under a pressure of eight atmospheres, by the addition of small quantities of antiseptics to the substratum, or by the passage of the organisms through the bodies of certain animals. Klein failed with Pasteur's vaccine to protect rodents: they seemed to have no immunity; if the vaccine acted at all, it caused splenic fever.

The attenuation is not accompanied by any morphological change; the virus "breeds true," and its virulence may be restored at any time.

Typhoid Fever.—Klebs, Eberth, Koch, and Meyer were the first to describe organisms in this disease. These organisms were figured as small bacilli with rounded ends. They were found in the intestinal lesions, mesenteric glands, and spleen. They were most numerous and therefore easiest to find during the first and second weeks of the disease. They stained badly with aniline dyes, and for a time these

observers worked with unstained specimens clarified by an alkali. Eberth was thus able to discover the bacilli in eighteen out of forty cases. Koch succeeded in staining the organisms with Bismarck brown, and demonstrated their presence in half the cases examined by him.

All these observers made control-observations on other cases, such as tubercular ulceration of the intestine; but they never found the typhoid bacillus in diseases other than typhoid fever. They sometimes found cocci in the intestine and glands, but regarded these as secondary.

A very important paper by Gaffky appeared in 1884. He started with the observation that the bacilli had been found in only half the cases examined. They must therefore have either disappeared before the disease, which they caused, had run its course, or else they were present, but not found. The latter alternative seemed probable, as they had been demonstrated in late stages in some cases, and missed at early stages in others. He pointed out that in typhoid fever the bacilli are not scattered everywhere, but are always in foci, and therefore more difficult to find.

Gaffky himself investigated twenty-eight cases, and, in twenty-six, demonstrated the presence of bacilli in parts other than the intestine —such as the mesenteric glands, spleen, liver or kidney. In one of the other two cases, the bacilli were found in a recently swollen, solitary follicle; and in the second, the intestines showed only healing ulcers.

In one case, which Gaffky does not include in his list, although it had been diagnosed as typhoid fever, both during life and at the post-mortem examination, immense numbers of cocci were found in the organs, and it was impossible to distinguish the typhoid bacilli. Gaffky throws out the suggestion that there may be a disease clinically like typhoid fever due to invasion of the intestine by cocci.

The earlier the case, the more numerous are the bacilli. If many are found in old cases, it is probable that a relapse has occurred.

Since that time many other observations have been published. The following is a summary of the results arrived at. The bacilli can, with some difficulty, be found during life in the fæces, spleen (obtained by puncture), and urine. After death, if the parts are removed without any delay, the organisms can be easily discovered in the intestines, spleen, liver, mesenteric glands, and kidneys. They occur in groups, but do not give rise to "tubercles." Their presence can be more

readily ascertained by inoculating a culture-ground with a piece of the suspected organ, than by examining stained sections under the microscope. They stain slowly and part with the colour easily. The best stains are probably Lœffler's methylene blue (p. 364), and Ziehl's fuchsine stain (p. 331). The bacilli do not retain the colour when treated by Gram's method (p. 330).

In appearance typhoid bacilli are not unlike tubercle bacilli. Their breadth is about a third of their length, which varies between 2 μ and 3 μ. Thus, they are a trifle thicker than tubercle bacilli, while their ends are distinctly rounded. Clear spaces often occupy the centre of the rods. There is some doubt as to the existence of spores. Those who believe in their existence describe them as rounded bodies, reaching right across the breadth of the rods, and lying at their ends. The chief microscopic features which distinguish typhoid from tubercle bacilli are the possession of flagella, the power of active movement, and some of the staining reactions. A typhoid bacillus, when stained by Lœffler's method, appears enveloped by a thick capsule. In intimate connection with this capsule, apparently composed of the same substance, and distributed over its whole surface, are the flagella, eight to twelve in number, varying much in length and thickness. Sometimes they are considerably longer than the parasite itself. Some of the bacilli are said to have only a single flagellum at one end.

Cultures can be readily obtained. The organism thrives in milk, and can even multiply for a time in sterilised drinking-water—points of practical importance. It does not liquefy peptonised gelatine, but produces in it roundish, slightly granular, yellow-brown colonies. It is mainly aërobic. Potato-cultures of this bacillus are almost invisible: this fact is utilised in the recognition of this organism. Thus, if a fresh potato-culture be incubated for forty-eight hours, *no visible change* occurs; but if surface-scrapings be then taken, stained, and examined, threads of the bacilli will be easily found. Other methods, none of which are absolutely characteristic, have been devised to meet the same difficulty. Singly, each is of little value; taken together, they are practically sufficient for the purpose of identification. Thus acid-products, but *no indol,* are formed in bouillon-cultures, while most bacilli, occurring under the same conditions, form indol. Another suggested test depends on the tendency which this organism possesses of *absorbing the colour,* when cultivated on a gelatine medium stained with gentian-violet, thus leaving the gelatine colourless. Still another is founded on a slight indifference which some organisms show to the

action of carbolic acid. Thus, if a minute quantity of carbolic acid (2·5 per 1000) be added to a culture of mixed organisms, the growth of most will be arrested, but *that of typhoid* and a few others *will continue.*

According to Sternberg, ten minutes' exposure to moist heat at 140° F. destroys typhoid bacilli: others give boiling point as the fatal limit, and state that "spores" will survive a temperature of 194° F. Brieger has separated from cultures some fatty acids, and a poisonous basic substance which he names "typhotoxin."

Inoculation has hitherto been only partially successful. It is doubtful if any animal is susceptible to typhoid fever as we know it in man. Rabbits, dogs and mice have been inoculated, and have died in thirty-six hours with symptoms of general septicæmia: but though enlarged spleens and swollen Peyer's patches have been very generally found, the disease never runs a longer course, nor is there ever any characteristic ulceration. Furthermore, almost precisely similar results have been obtained by injecting either the filtered products of the organism or the typhotoxin itself. In spite of this gap in the chain of evidence, all the observers quoted believe that this bacillus is the cause of typhoid; and we may, at any rate, affirm that it is constantly present in typhoid, is recognisable from all known bacilli by the various characteristics given above, and is not found in any other disease. Gaffky believes that infection always occurs through the mucous membrane of the intestine: even when the poison seems to have been inhaled as dust, he thinks it is caught on the mucous membrane of the pharynx, swallowed, carried through the stomach, and thus brought into contact with the bowel.

Bacillus coli communis (Bacterium coli commune).—This bacillus is a common denizen of the alimentary tract, and especially of the neighbourhood of the cæcum. It is also found in the mouth, and occasionally in other parts. It very rarely occurs alone. In size, in shape, in the possession of flagella, and in staining reactions, this organism very closely resembles that of typhoid fever. According to some observers, the B. coli communis has fewer flagella, but this supposed peculiarity is certainly not constant. There is a tendency for the bacilli to occur in pairs, and when cultivated, in short threads. This organism probably does not form spores. It is mainly aërobic, and seems to have a slight power of active movement. Like the typhoid bacillus, it grows best in acid media. It is easily cultivated, but the results are not sufficiently distinctive to be of much diagnostic value.

In gelatine tube-cultures it assumes the form of an irregularly encrusted stick, with small outgrowths here and there, but without tapering in either direction.

There can be no doubt, on the one hand, that this organism exists in perfectly healthy intestine ; nor any doubt, on the other, that in many diseased conditions, it is by far the most prevalent of the organisms present, and occasionally, perhaps, the only one that can be found. Hence it seems probable either that other bacilli are, at present, confounded with this one, or that this is subject to very great variations in virulence. There is a very general belief that, at any rate, the latter alternative is true, though the cause of this variation is quite unknown. In some states the organism seems able to produce a condition similar to septicæmia ; in others, only to give rise to local irritation and suppuration. Macaigne is of opinion that this organism is the chief causative agent in the following comprehensive group of conditions. The evidence on which he bases this opinion will be found in his very interesting monograph.* In no case does the evidence amount to absolute proof.

General diseases.—Cholera nostras, cholera infantum, certain obscure infective febrile disorders, and chronic enteritis with marked wasting.

Local diseases.—Dysentery, ulceration of the vermiform appendix, pylephlebitis, abscess in the liver or gall bladder, and peritonitis.

It has been suggested that the bacillus coli communis and the typhoid bacillus are identical. Besides the points of similarity already mentioned, it is found that when injected into the veins of rabbits and guinea-pigs, it produces a fatal disease identical with that already described as occurring when cultures of the typhoid bacillus are similarly introduced.

Diphtheria.—In 1883 Klebs drew attention to a bacillus which he had found constantly present in diphtheritic membrane. In the following year, Lœffler published a full account of its morphology and cultivation, together with results obtained by inoculation. Since that time, many workers have traversed the same ground, and the main facts concerning the organism have thus been fully proved.

The bacillus is to be found in all cases both of diphtheria and of membranous croup. It is limited to the false membrane and its neighbourhood, and grows most abundantly in the more superficial parts of the membrane. It is never found in any internal organ, though its presence in the membrane can be made out during all

* "Le Bacterium Coli Commune," Paris, 1892.

stages of the disease; while the examination of scrapings from the mucous surface of the mouth shows that it may continue to live a precarious existence for three weeks after the fever has disappeared. It is not found in any other disease—at least such is the conclusion of the vast majority of competent observers. Bacilli having a close morphological resemblance to it seem to be occasionally present in the mouths of healthy individuals, as well as organisms giving even the same culture-results as the diphtheria bacillus, but not possessing any pathogenic power. These may be attenuated forms of the original bacillus. Bacilli taken from diphtheritic membrane can be cultivated through many generations, and after an interval of some months are still capable, when inoculated, of giving rise to the original disease—not merely the local inflammation and membrane, but also the subsequent paralysis.

The diphtheria bacillus is generally rather shorter and thicker than the tubercle bacillus. It is usually from 1·5 μ to 2·5 μ long, and about a third as broad. Some observers have accredited it with a length of 6 μ to 8 μ, but they have probably included more than one individual in their measurement. Its shape is not always regular: sometimes the ends are thicker than the centre, and sometimes the centre than the ends. The latter are rounded. The bacilli not infrequently contain a row of two or three highly refracting areas, the nature of which is unknown. In all probability they are *not* spores. The organism is believed to multiply by fission only. It never forms long threads: it is motionless. Lœffler's alkaline methylene blue solution* gives the best staining results, but Gram's method can also be employed.

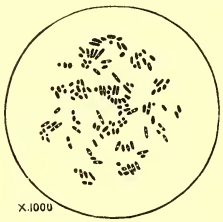


FIG. 126.—*Bacillus of Diphtheria.* (Lœffler.) (From a specimen by Dr. Arkle.)

The organism can be cultivated in many media. It does not liquefy gelatine. It grows well in milk; but the most frequently employed culture-ground is Lœffler's serum.† A minute portion of membrane, transferred to this, will develop, in the course of twenty-four hours, small grey elevated discs with pale circumferences. In secondary cultures these show a tendency to become arranged in lines (see

* Saturated alcoholic solution of methylene blue, 30 c.c.; solution of caustic potash of 1 : 10,000, 100 c.c. Lœffler's method of staining flagella is altogether different.

† Peptone, 1·0; grape sugar, 1·0; chloride of sodium, ·5; neutral gelatinised veal broth, 100·0; blood serum, 300·0.

Frontispiece). Growth can take place at any temperature between 70° F. and 108° F. but is most luxuriant when it remains between 92° and 99° F. Moist heat of 140° F. is fatal to its life. A free supply of oxygen encourages but is not essential to its growth. There is no difficulty in maintaining the virulence of the organism during cultivation; but if a culture be left undisturbed for some months its virulence diminishes, and this result follows much more rapidly if it be allowed to become acid. In either case replantation into a fresh culture-ground rapidly restores the virulence. The organism resists drying to a much greater extent than is usual in non-spore-bearing bacilli. If a specimen be dried and kept dry for six months, it will grow as soon as it is

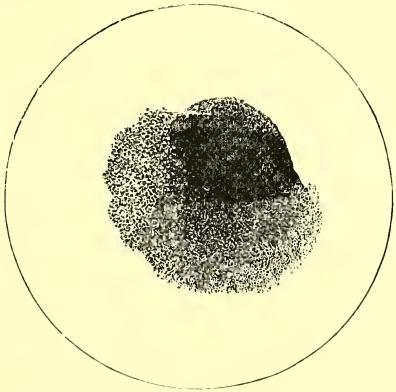


FIG. 127.—*Bacillus of Diphtheria.* Colony on agar twenty-four hours after inoculation. × 100. (After Fränkel.)

placed under favourable conditions. This point is of great practical importance, and emphasizes the necessity for thorough disinfection.

In 1890, by means of filtration through porcelain, and subsequent precipitation with absolute alcohol, Roux and Yersin succeeded in isolating, from cultures of the organism, a poison, which if injected into animals in large doses caused prostration and death, but if in small doses only paralysis and albuminuria (in rabbits on the fifth day). In no case was any membrane formed. It was also noted that the addition of acid to the poison rendered it harmless. They believed this poison to be an "unformed ferment."

Two years later, by very similar procedures, Sidney Martin separated identical series of substances (1) from the tissues of persons dead of diphtheria; and (2) from cultures of the organism on media closely

resembling those of the tissues (p. 340). This series consisted of hetero-albumose, proto-albumose, deutero-albumose, and an organic acid. Of these, the first was only to be obtained from the membrane, and the last from the tissues; the proto- and deutero-albumoses were present in both membrane and tissues. Martin showed that the factory of the albumoses was the tissues and especially the spleen; and that but little was formed at the site of the membrane. He regarded all the products as the result of a ferment produced at the seat of the local disease, and thence entering the circulation. He showed that the paralytic effects were due to the action of the albumoses on the peripheral nerves, which caused breaking up of the myelin sheath, and more or less thinning and even disappearance of the axis-cylinder: fatty degeneration of the heart and voluntary muscles were also found (p. 320).

From the foregoing account it will be seen that the requirements of the organism as regards air, temperature, and moisture are admirably provided for in the mouth and upper air-passages. Moreover they are supplemented by the co-operation of various cocci, especially the pyogenic varieties, which are always ready to hand. The spread of the membrane inwards is probably due partly to the more suitable temperature and partly to the force of inspiration.

Another step in advance was made in the same year (1892) by Behring, who drew attention to the acquired immunity which could be obtained against these diphtheria bacilli. He described four ways by which animals could be rendered immune. He injected (1) cultures of the bacillus attenuated by heat; (2) cultures attenuated by the addition of trichloride of iodine; (3) the pleural exudation of animals dead of experimental diphtheria; or (4) a dose of virulent diphtheria bacilli, followed by one of trichloride of iodine. He next showed that the addition of some serum, from an animal thus immunised, to an ordinary culture of the organism not only killed the bacilli but neutralised the poison as well, so that, when injected, it was found to be innocuous. The final stage was reached when he showed that if a fatal dose of diphtheria poison had been injected, it could be neutralised by a subsequent injection of this "immunised serum." A good deal was found to depend upon the method employed for rendering immune the animal from which the serum was taken. Within certain limits, the injection of small amounts, spread over a long period, was found to give the best results. The principles, determining the dose of "immunised serum" or "antitoxin," are not yet understood. Does the

"anti-toxin" simply neutralise the chemical poison, or does it induce action on the part of the tissues? In cases in which only the filtered culture and not the actual bacilli are employed, the dose of serum required is found to vary not only with that of the poison, but also with the body-weight and possibly with the species of animal employed. Again, the doses requisite depend upon the interval between the two injections. It was smallest when that of the serum immediately followed the poison. These results have led to the extensive use of the immunised serum for therapeutic purposes: these have been more fully referred to in the section on Immunity (p. 344).

Influenza.—In 1892, Pfeiffer, Kitasato, and Canon succeeded in finding a minute bacillus, which they believe to be the cause of this disease. It is extremely minute, measuring ·5 μ by ·2 μ; that is, it is about half the size of the bacillus of "mouse-septicæmia." It stains with Ziehl's and Lœffler's fluids: the ends take the stain best, and thus the organism often looks like a diplococcus. It occurs singly, in pairs, and in short chains. Large numbers have been found in the bronchial secretion: they disappear with the catarrh. It has also been demonstrated in the blood. In that fluid it is either less frequently present, or more difficult to stain. It has been found in the peri-bronchial tissue.

Pure cultures are not easily obtained. On sugar-agar these appear as small, discrete, transparent globules visible only with a lens. The bacillus is aërobic, grows best at the body temperature, and is easily destroyed by drying.

Local inunction of pure cultures into the respiratory mucous membrane of monkeys and rabbits is followed by the disease.

The Plague (Bubonic Fever).—In a preliminary communication,* Kitasato has described his researches during a recent epidemic at Hong Kong.

(1) He succeeded in finding bacilli in the blood, buboes, and internal organs of the plague-stricken patients. The organisms stained readily with the usual reagents; they had rounded ends, which appeared darker than the central parts; they possessed slight power of movement. No spores were discovered. The organisms were easily destroyed by sunlight, heat, carbolic acid, and quicklime. Similar organisms were never found in healthy persons, or in those suffering from any other disease.

(2) Cultures were obtained on blood-serum, glycerine-agar, and

* *The Practitioner*, October 1894.

other media. The colonies were whitish-grey, rounded patches, with uneven edges. In the cultures the bacilli often formed long threads.

(3) Mice, rats, guinea-pigs and rabbits, if inoculated with pure cultures or with blood from patients, succumbed with a constant sequence of symptoms. Roughly speaking, these appear to have corresponded to those in man, though the enlargement of the glands does not seem to have been so marked. The bacilli were found in the blood, glands, and organs of these animals. Pigeons are immune. Animals, fed with the organism or blood, died in the same way as those inoculated.

Septicæmia of Mice.—Koch injected putrid fluids beneath the skin of mice, in quantities too small to cause septic intoxication. A peculiar disease, without abscess-formation, occurred in some cases, and was transmissible with certainty to others by inoculation of a very small quantity of blood. Extremely small bacilli, chiefly in leucocytes, were shown to be the cause of the disease. One attack confers immunity. It is not inoculable upon field-mice, guinea-pigs, or chickens (see "Septicæmia.")

Tetanus.—In 1884 it was shown that tetanus was an inoculable disease. In the same year a special bacillus was described, but it was not isolated and cultivated until 1889. Kitasato accomplished these results by heating the impure cultures of pus, obtained from the original wound, to a temperature of 80° C. (176° F.), and then incubating the residue in an atmosphere of hydrogen.



FIG. 128.—*Bacillus of Tetanus.* For description, see text.

The bacillus thus obtained is very small. It is generally arranged in longer rods (3 μ to 5 $\mu \times \cdot 4\ \mu$). Spores are often found. They occupy one end of the bacillus, and being two to four times the diameter of the organism, give it the appearance of a miniature drumstick (Fig. 128). One or two flagella at the opposite end are described by some observers. The bacillus can be stained by the usual methods. Its habitat seems to be the superficial soil, from which it can often be obtained.

It can be readily cultivated if great care be taken to exclude oxygen: this bacillus and that of malignant œdema are the two most prominent examples of anaërobic organisms. The tetanus bacillus liquefies gelatine slowly, and grows only beneath the surface. The most suitable temperature is 97° F. to 100° F. The cultures have a characteristic odour. The spores are noted for the great resisting power they show to the ordinary methods of destruction. Thus, they have been known to resist successfully *boiling* for five minutes, *drying* for five months, and immersion in *carbolic acid* (1 : 20) for ten hours, and in *mercuric chloride* (1 : 1000) for three hours. Fifteen minutes boiling is invariably fatal. For a long time, all attempts at attenuation failed, but it has lately been shown by Tizzoni and Cattani that attenuation results from (1) the exposure to the air of spores on threads; and (2) the preservation of cultures in various gases for long periods—generally over a year.

The constant presence of the bacillus in cases of tetanus, and the possibility of purifying it by cultivation, having been established, it remained for Kitasato to complete the proof by successfully inoculating these cultures on animals. He showed not only that inoculation of the bacillus produces the disease, but also that in such cases the organism remains confined to the wound, and that the symptoms are due to the absorption and circulation of their products. Thus, he found (1) that inoculation of a *sterilised* culture produced a fatal form of the disease, but that no bacillus could be found in, and no cultures obtained from, the organs of an animal killed in this way; (2) that inoculation of an *unsterilised* culture produced a similar disease, and, similarly again, that no bacilli could be found in, and no cultures obtained from, the *distant* organs; and (3) that in the latter case the symptoms were first observed in the locality of the inoculated part. He concluded, therefore, that the bacilli in the wound produced their effect by manufacturing poisons which are gradually disseminated.

The first of the products separated was a crystallisable substance known as *tetanine*, while the second was called *tetanotoxine*. The third, in order of discovery, though the most poisonous of the three, has been named *tetanus toxalbumose*.

Kitasato conferred a two-months immunity on rabbits by injecting a small portion of a sterilised (filtered) culture, followed by five daily injections of trichloride of iodine (3 c.c. of one per cent. solution). Subsequent observers have obtained results precisely analogous to those already described in diphtheria. Small but regularly increasing (3 c.c.

to 120 c c.) and repeated doses of the filtered cultures gradually confer immunity; and the serum obtained from animals thus protected is found to prevent the development of symptoms if injected *before,* or *with,* a fatal dose of the toxines. By some observers the same result is claimed when the injection *follows* the development of the symptoms of the disease. The efficacy of the "antitoxin" serum, when kept in tubes, lasts little more than a week.

Malignant Œdema.—A spreading œdema ending fatally may be produced by inoculation of mice, guinea-pigs, or rabbits with garden mould. One form of bacillus develops, and the œdema-fluid containing it is easily inoculable (p. 326). The bacillus is 3 μ to 3·5 μ in length, but grows into longer threads, which much resemble anthrax bacilli. They differ in showing no segmentation, in having rounded ends, and in being absolutely anaërobic. In cultures, characteristic air-bubbles occur at the sides of the tube (see Frontispiece).

SPIROBACTERIA. — Two diseases, Relapsing Fever and Cholera, are associated with curved organisms belonging to this order.

Relapsing Fever.—The *Spirochæta Obermeieri* (Fig. 121, p. 347), often called spirillum, is found in the blood in this disease. It was discovered by Obermeier in 1873. It is a zigzag, sharply curved, uniform thread, 16 to 40 μ long, with quick undulating movements. No spores are known. The organism takes the ordinary stains feebly, and does not retain the stain when treated by Gram's method. The organisms appear in the blood soon after the commencement of an attack, and disappear with remarkable speed after the crisis. Metchnikoff states that during the afebrile interval they accumulate in the spleen, and Soudakewitch has shown that the previous removal of this organ enormously increases the mortality. Nothing is seen of them till the relapse, when they return. All attempts to cultivate them have hitherto failed. The disease has been inoculated from man on man, and from man on apes (Carter, Koch). It is said that blood taken in the fever-free period is not infective.

Cholera.—The infective nature of cholera has long been maintained by many observers, but nothing definite was known in 1883, when Koch began his work in Egypt and India. He was at once struck by the discrepancy between the accounts of the *post-mortem appearances* as given in text-books, and the conditions which he actually found. He observed that it was quite rare to find the intestinal mucosa simply opaque with slightly swollen follicles and the

intestinal contents like gruel, as had been described. He found that this happened only in the most acute cases, and that the gruel-like contents then consisted of an almost pure cultivation of the parasite presently to be described. Koch only very exceptionally found in the intestines any fluid so thin as to be comparable with rice-water. In cases of somewhat longer duration, he found the follicles and Peyer's patches surrounded by zones of hyperæmia, running together into red areas; and ultimately, in the longest cases, the small intestine became intensely congested, the congestion being most marked above the ileo-cæcal valve and dying away in the upward direction. With these changes the intestinal contents became increasingly bloody, and finally exhaled a distinctly putrefactive odour, whilst the parasite, above referred to, was more or less replaced by other bacterial forms.

In the stage of patchy redness, sections of the mucosa parallel to its surface showed that, in the most acute cases, the redness corresponded to an invasion of the epithelium of the tubular glands by the parasite found in the intestine: the organisms were found lying between the epithelium and the basement-membrane. This bacterium, therefore, soon attracted attention by its definite form and by its apparent constancy.

Koch's Cholera Spirillum or *Vibrio* is about one-half to two-thirds the length of a tubercle bacillus, but thicker (about ·5 μ). It is curved, usually to a degree equal to that of a comma (hence the first name—comma-bacillus), but sometimes to that of a semi-circle. It multiplies by transverse division, and, when the organism is grown upon gelatinous media or the intestinal mucosa, the segments separate from each other at once; if two remain united, they form an S (Fig. 129), their curves being in opposite directions. When cultivated for any length of time in nutritive fluids, the spirilla may remain united until they form delicate spirals of some length, very like the spirillum of relapsing fever: these are probably degenerative forms. A single flagellum is usually attached to one end of each organism. Occasionally two or more flagella may be similarly attached. More rarely still, flagella may be connected with both ends. Both single cells and spirals are actively mobile. When present in the intestines, in large numbers, they form, according to Koch, little heaps in which the single cells have all the same direction; so that it looks as if a little swarm of them were making their way, one behind the other, like fish in slowly moving water (Fig. 129). The organisms stain with the

ordinary solutions before mentioned, but do not retain the colour when treated by Gram's method.

The vibrio grows well upon all the ordinary media, and its rapid multiplication can be watched in a drop of meat-infusion upon the under surface of a cover-glass. If linen, stained with cholera-dejecta, be kept moist and exposed to the air, growth is also very free for two or three days. The colonies upon nutrient gelatine or agar begin as very pale tiny spots, which, as they get larger, present a slightly irregular outline and a finely granular surface: Koch compares them to heaps of fine bits of glass. On the second day the gelatine liquefies



FIG. 129.—*Cholera Spirilla.* Flagella not shown.
(From a specimen by Dr. Arkle, prepared in Koch's Laboratory.)

in the immediate neighbourhood of each point, and the colony sinks into a bell-shaped depression with a white apical point. The appearance of a long narrow funnel is very typical when a tube is inoculated by puncture (see Frontispiece). In the case of allied organisms, liquefaction generally takes place more rapidly. For diagnosis, Koch relies on the combined evidence afforded by (1) the microscopic appearances; (2) the results of cultivation on gelatine and on agar; (3) the indol reaction with peptone-cultures; and (4) the effects of inoculation on animals.

The growth of this spirillum is unusually rapid; it reaches its limit in a few days, remains a short time stationary, and then diminishes, the bacilli either shrivelling or swelling, and staining more or less

imperfectly. Many strange "involution-forms" appear: these have been thought to belong to different species. Clear spots failing to stain have often been taken for spores; but Koch showed that spirilla containing these spots were obviously dying, for they failed to grow, and did not possess the resisting power of spore-bearing organisms. He does not believe that spores are formed; but Hüppe and others have described the splitting up of vegetative cells into small fragments, which become rounded, like spores: these, when transplanted, grow into spirilla (*arthrospores*).

Growth is most rapid at 86° F. to 104° F. (30° to 40° C.), and stops below 60·8° F. (16° C.). Death results from exposure to a moist temperature of 131° F. (55° C.). Oxygen is essential to *growth*, but neither its absence nor an atmosphere of carbon dioxide causes death. An alkaline reaction is most favourable to growth, while distinct acidity often arrests it; but all acids have not this effect, for though the surface of a potato is acid, yet growth occurs freely upon it. Koch added many antiseptics to cultivations, to discover those which most powerfully hindered development. Quinine (1 : 5000) and mercuric chloride (1 : 100,000) head the list, but it is obvious that the constitution of the material to which they are added will greatly affect the result. Koch's most important observation on this point was that *complete* **desiccation** killed the vegetating cells of these bacteria in three hours. It must be remembered that in pappy substances many hours may be required to complete desiccation, but, even in such, twenty-four hours suffice to destroy cholera-germs. On the other hand, Hüppe obtained fresh cultures from arthrosporous spirilla after four weeks' desiccation; and vigorous growths have been obtained from desiccated cultures after ten months. It is not yet certain, but Hüppe believes that arthrospores were contained in the latter, and that new growths after long intervals always arise from these structures. Lastly, it is very probable, if not certain, that this spirillum soon dies in putrid fluid, cesspools and the like, and that consequently the addition of antiseptics to such collections of matter may possibly preserve rather than destroy the cholera-germ.

Koch was strongly of opinion when he wrote his early papers on this subject, that the form of the "comma-bacillus" was quite characteristic: but Finkler and Prior discovered a spirillum very like it in "English cholera;" Denecke found another in cheese; Escherich obtained one from the alvine discharges of infants with summer diarrhœa; and Metchnikoff, one from fowls suffering from a special

form of enteritis. Koch found a bacterium like it, but thicker, in the water of the Hooghly. Careful study of the plate and tube cultivations of these very similar organisms and of their pathogenic effects, has shown that they can be readily distinguished by thoroughly competent observers.

It would seem from the above morphological and physiological details, that Koch's cholera-germ is a perfectly distinct organism; and that it is invariably present in the early stages of the disease. Yet all of Koch's statements are not fully accepted. Some observers affirm that the spirilla do not necessarily invade the intestinal epithelium. Gruber maintains that variations in the size, curve, sharpness of ends, and number of flagella are common, and depend on the special epidemic in question, on the conditions of growth, and on the stage of cultivation.

Koch's theory as to its action is that, being confined to the intestine, it produces a virulent general poison which is absorbed, and at the same time acts as an intense irritant to the mucous membrane. Early death in collapse, perhaps before the passage of a single stool, may result from general poisoning, and it is in these cases that the intestine is found pale—simple hyperæmia having died away. In longer cases the local effects become more marked, and increasing extravasation of red corpuscles remains to indicate the existence of the hyperæmia. Then the cholera-germ having reached its limit of development, hindered perhaps from further growth by the products of its own action, is more and more replaced by putrefactive germs, the products of which are both extremely irritant and poisonous. Various toxic bodies have been obtained from cultures of the cholera spirillum. These, when injected, give rise to cramps, cardiac failure, and lowered temperature, respectively. The exact nature of these is at present unknown.

Koch examined the intestinal contents and stools of a large number of cases—dysentery, intestinal catarrh, ulceration, typhoid and typhus, diarrhœa of adults and children; the stools of animals—normal and after arsenical poisoning; the contents of the Calcutta drains; and water from the most varied sources. Once only, in a tank in a cholera district, was the spirillum found external to the body, and here it seemed to have a clear relation to the epidemic around it. Koch therefore concludes that *this spirillum occurs only in cases of cholera.* Its discovery, therefore, in the stools of diarrhœa would be most important.

Metchnikoff has pointed out that, during a neighbouring epidemic of cholera, the drinking water of Versailles contained the cholera

vibrios, yet that those who drank the water remained unaffected. He has further shown that the organism persisted in the water for months after the epidemic had ceased, and therefore that the appearance of the microbe in water did not necessarily involve the appearance of an epidemic. He believes that cholera organisms may exist for some time in the intestines of animals without producing cholera. This result he attributed to the action of contiguous and contemporary organisms. Some of these aid, while others hinder, the action of the cholera vibrios.

In the proof of causation we have now shown :—

(1) That Koch's cholera spirillum is a specific organism to be found in all cases of cholera, and rarely, if ever, in persons not suffering from the disease.

(2) That pure cultures of the spirilla can be obtained ; but that successive cultivations tend to cause their degeneration.

The possibility of inoculating the disease must now be considered. By an accident, cholera-dejecta became mixed with water : this was drunk by seventeen persons ; of these, five had cholera (Macnamara). Again, at Berlin, during a course of demonstrations upon the bacteria of cholera, one of the members of the class was attacked by a distinct though mild form of the disease, his stools containing numbers of spirilla. No other source of infection seemed possible.

Meanwhile, Nicati and Rietsch at Marseilles succeeded in infecting dogs and guinea-pigs with a disease like cholera, by injecting cultivations of the spirilla into the duodenum ; and their results were repeated and confirmed by Koch and others. This method was adopted to avoid the stomach, in the acid secretion of which the cholera-germs ordinarily perished. Of eighteen guinea-pigs thus treated, thirteen died of "cholera;" whilst of "control" animals, injected with other bacteria, none died.

Koch next *neutralised* the gastric juice for about three hours by a suitable injection of carbonate of sodium, and, later, injected spirilla in meat-infusion, but with a negative result. He next delayed peristalsis by means of opium, with the result that of thirty-five guinea-pigs infected through the stomach, thirty died of "cholera."

Infection through the stomach would apparently be much easier in man than in guinea-pigs. Ewald finds that water introduced into an empty stomach remains neutral, or even becomes slightly alkaline : its quantity decreases slowly for an hour or more ; then decreases suddenly—evidently from opening of the pylorus—before its reaction

has become acid. Cholera spirilla, introduced shortly before this juncture, might reach the duodenum alive. If arthrospores exist, this is even more likely. It would therefore seem possible that the cholera spirillum might occasionally pass through the stomach of man without predisposition. As with other acute specific diseases, of those exposed, but few take the disease; and, according to Koch, almost all these had digestive troubles, gastro-intestinal catarrh, or an overloaded stomach—the latter condition diminishing the general acidity of the stomach and enabling the spirillum to pass with undigested masses.

The *contagion* of cholera *exists in the dejecta,* and quite exceptionally in vomit (when this has regurgitated from the intestines). For *spread* to occur, moisture is essential—as desiccation as a rule (see above) means death; cholera, therefore, does not, like tubercle, spread by the shaking of dust from linen; it is not carried by post nor by merchandise, but by man. As a rule, it is spread by the infection of water: this occurs very easily in India, where a large tank is employed to collect water for many people; and the one tank is used indifferently as a public bath, a wash-tub, a cesspool, and a reservoir of drinking water. Koch quotes convincing examples to show that the supply of pure water will prevent the occurrences of the disease where previously it has been rife. Moist provisions may be infected by contaminated hands or perhaps by flies.

It has already been shown that *this parasite can multiply apart from the body—e.g.,* on moist linen, on potato, or in meat-infusion. As it requires rather concentrated nourishment, it probably does not multiply in ordinary running water; but many of the rivers of India are extremely foul, and organic matter increases greatly where the waters stagnate, drains and gutters enter, and vegetable and animal refuse collects: round about such masses water may be muddy from germs. Stagnant surface-water, therefore, seems to be the great culture-ground for cholera-germs external to the body.

All evidence goes to show that *the home of the cholera-germ* is the delta of the Ganges—a region so peculiarly adapted to the growth of micro-organisms, by the quantity of dead animal and vegetable matter, and by the heat and the moisture, that one might expect to meet with quite special forms of bacteria. To this region careful inquiry has always been able to trace epidemics of cholera.

For an account of preventive vaccination against cholera, see p. 344.

The Blastomycetes or Yeasts.

These are small, round or oval cells, which multiply by budding (gemmation). Sometimes the cells cohere and form branching chains. When food is not abundant, as in the case of potato-cultivations, one to four spores may form in the interior of the yeast-cells; these develop when placed in fermentable fluids. Under the same conditions unjointed mycelium may be produced. Furthermore, when it is remembered that the growth of some higher fungi (*e.g.*, Mucor Mucedo) under *exceptional* circumstances is the same as that of yeasts under *ordinary* circumstances—*i.e.*, by gemmation, it seems possible that yeasts may really be vegetative forms of higher fungi.

Yeasts are of importance only as causes of fermentation. They never invade living tissues. They are common in the stomach either alone or in company with sarcinæ. They are frequently found in diabetic urine, but not at the time it is passed.

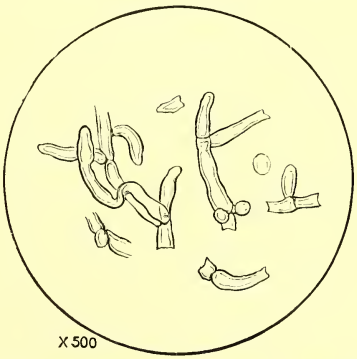


FIG. 130.—*Oidium Albicans.* Cells and spores seen on the surface of epithelium, scraped from an "aphthous" patch on an infant's tongue.

Thrush.—In this disease, tolerably adherent grey or milky patches form in the mouth, pharynx, and gullet, either of children at the breast, or of adults exhausted by wasting diseases (typhoid, phthisis). These patches are due to the growth of the **oidium albicans**, a parasite which was regarded as a mould; but Grawitz states that, when cultivated, this fungus shows itself to be a yeast, and probably the Mycoderma vini, which he has proved capable of growing on mucous membranes. The patches consist of tortuous, often branched filaments, formed of long cells united end to end, and distinctly constricted where they join. The filaments end in roundish cells, which produce one or more spores: these form heaps in the epithelium (Fig. 130).

The Hyphomycetes or Moulds.

These consist of filaments (*Hyphæ*) formed by a single row of cells placed end to end, growing by means of an apical cell which elongates and divides transversely. Lateral offshoots are common, but dichotomous branching is rare. The thallus may consist of a single hypha; but usually the hyphæ are numerous, and intercross loosely or closely. All spring from an axis or *germinal tube* which grows directly from a germinating spore. Compared with that of bacteria (p. 308), their growth is extremely slow.

In the adult plant the hyphæ are of two kinds (1) the *nutritive*, which grow into and extract nourishment from the culture-soil, forming in it, by their interlacement, the *mycelium;* and (2) the *reproductive*, which spring from the mycelium, and stand up from the substance in which the mycelium lies: these are called fruit-hyphæ. They are simple or branched, and bear at their ends spores or sexual organs. Reproduction is either asexual or sexual: the two methods may occur together on the same plant, or may alternate regularly or irregularly. Spores are formed by each—round, oval, or cylindrical, smooth or irregular, coloured or colourless; most are motionless, but some "swarm." Each consists of a little mass of protoplasm, surrounded by an envelope, which is made up of an outer (*exosporium*) and an inner (*endosporium*) layer: the exosporium is often pigmented. All spores have great power of resisting the action of physical and chemical agencies, and retain life for long periods; those formed asexually are ready at once to germinate, but those due to a sexual process almost always require a rest. The latter are the true *resting-spores;* but this name is often applied to all spores capable of retaining life for long periods in spite of adverse conditions.

To understand the above and what follows, the student should examine a few moulds from the surface of thin jam, paste, decaying fruit, or the surface of a slice of potato which has been exposed for an hour or two in a dwelling-room. In all, the aërial portion is easily studied, and the mycelium is readily shown by crushing a bit of the culture-ground under a cover-glass.

Asexual spore-formation occurs in three ways:—

(1) Hyphæ spring from the mycelium, and perhaps branch. The terminal cells divide transversely into spores (*conidia*), which either fall away singly or form chains.

(2) A hypha (*sporangiophore*) stands up from the mycelium, and its

end swells into a ball full of protoplasm, which segments and forms conidia (*sporangium*).

(3) From the surface of a knob on the end of a hypha (*conidiophore*), peg-like processes (*sterigmata*) sprout, each sterigma, by growth and transverse division, forming a chain of spores.

Sexual reproduction occurs in three ways :—

(1) **Conjugation.**—The apical cells of two hyphæ meet end to end, and blend into one cell (*zygospore*). From this, after a longer or shorter rest, a sporangiophore sprouts, and from its spores new plants grow, as in Mucor.

(2) **Fertilisation.**—(*a*) The end of a hypha becomes twisted like a corkscrew, more and more closely, until the turns form a continuous tube—the *ascogonium*. From the lower turns spring fine branches, one of which (*antheridium*) conjugates by its apex with the ascogonium ; the others simply cover the ascogonium continuously, and are converted by division into polygonal cells, which form a capsule (*perithecium*) round it. Many tranverse septa form in the tube of the ascogonium, and from the cells thus produced flask-shaped lateral projections (*asci*) develop : in each of these, eight spores generally appear. The perithecium thins as the asci enlarge, the walls of the asci disappear, and an easily ruptured sphere of spores remains. When these germinate the endospore swells, splits the exospore, and throws out the germinal tube, whence springs the mycelium. This again gives origin first to conidiophores, then to perithecia. Eurotium repens, and Aspergillus glaucus, found especially on preserved fruit, show these changes (Sachs).

(*b*) In some species, certain cells form an organ (*oogonium*), in which one or more female reproductive bodies (*oospheres*) are formed ; whilst other cells form a male organ (*antheridium*) in which *spermatozoids* are produced. The oosphere, which is hundreds of times larger than the spermatozoids, remains in the oogonium, and is there fertilised by the mobile spermatozoids. It is now called an *oospore*, and may, after a rest, directly develop into a new plant, or form cells, each of which develops in like manner.

Conditions of Life.—Food.—Possessed of no chlorophyll, moulds are unable to build up carbon-compounds. They assimilate those built up by other plants or animals. They are therefore always either saprophytes or parasites : in the latter case they may kill their host. They require a free supply of oxygen ; but some can obtain it, at least for a time, by decomposition of organic compounds like sugar.

Thus, Mucor racemosus, cultivated on the surface of a saccharine liquid, absorbs oxygen, oxidises completely some of the sugar, exhales carbon dioxide, and grows rapidly. If deprived of oxygen, as by immersion, only the mycelium grows, and this becomes broken up into short cells, which multiply by budding, and much resemble yeast-cells. The growth is much slower, carbon dioxide escapes in bubbles, and alcohol appears in the liquid. But all these changes soon cease, and the process can be started again only by a fresh supply of oxygen (Duclaux). Some moulds, as Penicillium glaucum, Aspergillus niger, have no power of thus obtaining oxygen, and die if cut off from the free gas. The change in the character of growth above-mentioned, accompanying changes in conditions of life, is often pointed to as evidence in favour of the mutability of bacteria.

Light.—Many moulds can develop completely without light: some require it for the discharge of spores and other processes.

Temperature.—Ziegler states that moulds flourish best at temperatures *below* that of the body, and that some will not grow at all at so high a temperature. A few species of Aspergillus and Mucor grow well between 95° and 105° F. The spores are as resistant to external agencies as are those of bacteria.

Water is essential, but mere dampness is sufficient.

Action.—Moulds are associated with processes of *rotting* or *decay.* The peculiar smell and taste which they impart is known to all. The products of their life-action have not been closely investigated; but they are neither very poisonous nor very irritating, so far as *human* tissues are concerned.

Distribution.—The spores of moulds are much more numerous in the air than are other organisms. They, therefore, constantly fall upon the skin and enter the air-passages with air, and the food-passages with food. As a rule, they find no nidus suitable for their development: the supply of free oxygen is often insufficient, and the temperature too high. Certain of them, however, when brought into contact with accumulated inflammatory discharges, or with sloughs, take root and fructify. This is most likely to occur in the nose, mouth and pharynx. They are here saprophytes, but the products to which they give rise may irritate the living tissues lying beneath the soil in which they grow. Species of Mucor and Aspergillus are those commonly found.

Pathogenic Moulds.—Owing to the peculiarities mentioned in their life-history, these fungi have but little power of invading living

tissues. Certain skin-diseases are, however, due to the growth of species of this class in epidermic structures: they are (1) *favus;* (2) *tinea tonsurans, t. kerion, t. circinata, t. sycosis,* and *t. unguium;* and (3) *tinea versicolor.* Two diseases, *actinomycosis,* and the *Madura foot* of India, have been attributed to penetration of the deeper tissues by hyphomycetous fungi, and true mycoses may also occasionally be due to growths of the *Aspergillus fumigatus* or *A. niger.*

Favus.—The *Achorion Schönleinii* forms almost the whole of the light, yellow, mouldy-smelling crusts characteristic of **Favus.** When in hairy parts, which are the usual seats, the hairs are always invaded, especially the roots. Here the parasite grows luxuriantly, but it does not extend far up the shaft; its primary seat is the epithelium of the hair-follicle. On non-hairy parts, the mycelium invades the *deeper layers* of the *epidermis,* and may even penetrate to the corium: in this case the local irritation will be more marked. The mycelium consists of unjointed, branching, confusedly intercrossing tubes; in certain of them, which become divided into joints, oval spores form.

The nails are very rarely invaded; and then only by mycelium.

Tinea Tonsurans. — The *Trichophyton tonsurans* is generally assumed to be the one parasite common to tinea tonsurans, tinea kerion, tinea circinata, tinea sycosis, and tinea unguium. Different varieties have lately been described. These are distinguished by the size of the spores (*t. megalosporon, t. microsporon*), their pyogenic effects (*t. megalosporon*), and their culture-results (Sabouraud). These forms are not found growing together.

When the hair is affected, the root and the lower part of the shaft are crammed with spores, lying in rows between the fibrils of the degenerate hairs which are opaque and brittle. It is doubtful how far the fungus makes its way down between the shaft and the wall of the follicle before it penetrates the former. The hair breaks just beyond the scalp, leaving a stubbly line of split or twisted ends. Epidermic scales from the surface of the scalp may contain the fungus, but the deeper living cells of the root-sheaths are always free from it (Thin and Taylor). Spores are abundant, and oval in shape; mycelial threads are rare. Points worth remembering in connection with the undoubted fungoid origin of the disease, are (1) its usual limitation to children; (2) its tendency to fasten upon the weakly; (3) its great contagiousness when acute, diminishing as it becomes chronic; and (4) its greater severity when contracted from animals, as the horse

(Tinea megalosporon). It may excite severe irritation and even sup puration—**T. kerion.**

Tinea circinata. — Here the parasite infests epidermic cells, always causing desquamation, sometimes vesiculation, or even more severe inflammation. It spreads uniformly from the point at which it first takes root, and consequently assumes the form of a gradually enlarging circle. The central parts of the fungus die, and the circumferential give rise to hyperæmia in their neighbourhood. Mycelium is present chiefly in the form of very long, jointed and branched threads; the spores are scanty, single, or in short chains. The fungus altogether is often scanty, and is especially difficult to detect if it has excited inflammation.

Tinea sycosis.—(*Tinea megalosporon*).—When attacking the beard the fungus is found chiefly in the hair, but also in the follicle; both mycelium and spores are seen, the latter in excess, but not so markedly as in T. tonsurans. The mycelium generally lies round the root of the hair, and is pulled out of the sheath with it. Severe inflammation is generally excited.

Tinea unguium.—Mycelial threads of trichophyton may occasionally invade a finger-nail, rendering it opaque, thick and brittle. Unlike a general condition, the fungus produces these changes in two or three nails only, and the toe-nails are scarcely ever affected. In this situation it is extremely difficult to destroy.

Chloasma, Pityriasis versicolor.—*Microsporon furfur* invades the horny layer of the epidermis of covered parts of the trunk, growing more superficially than any of the above, rarely causing irritation and not attacking nails or hair. It consists of jointed mycelial threads, which are always abundant; and spores, which vary in form, lie in groups and grow at the ends of the mycelial threads. It can be easily cultivated.

Actinomycosis.—The ray fungus (*actinomyces*) is believed to be the cause of this disease. Its description will be found in the chapter on "Infective Granulomata." Its botanical position is doubtful.

Madura Foot.—*Mycetoma.*—In certain parts of India the feet of the natives are liable to a peculiar swelling; "tubercles" form beneath the skin, burst, and leave sinuses from which bodies, like those constituting the roe of a fish, are discharged, or, more rarely, bodies like

grains of gunpowder. In the latter, fungous elements have been recognised, and called *Chionyphe Carteri*. These are believed by some to be the cause of both classes of the disease. On section, masses of the above bodies are seen, especially in the fatty layer; the masses may have no obvious communication with each other, or with the surface. The botanical position of the fungi found is doubtful. Kanthack considers the disease a form of actinomycosis. Boyce and Surveyor acknowledge the similarity, but not the identity, of the two.

CHAPTER XXII.

THE INFECTIVE GRANULOMATA.

The term *infective granulomata* is applied to a group of diseases, including tubercle, lupus, syphilis, glanders and farcy, leprosy, actinomycosis, and rhinoscleroma. It was originally used by Virchow to emphasize the points of resemblance which the lesions of the above diseases show to some forms of tumour. These lesions consist of cells, varying between lymphoid and giant-cells in size, and lying in a scanty matrix; while the mass thus formed presents to the naked eye a more or less defined outline. The lesions therefore resemble sarcomata in structure. Many of them develop without any obvious cause, and are not accompanied by any distinct signs of inflammation; they often *persist* for long periods, and, with the exception of gummata, rarely undergo absorption; they often *degenerate* early, and show little tendency to develop into a permanent tissue; and lastly, most of the lesions have an *infective* power, reproducing themselves in neighbouring or distant parts by both blood and lymphatic vessels. In all these respects the above-mentioned new formations resemble malignant tumours, but they differ from them ætiologically. In the case of some it is certain, and in the case of all it is probable, that the tumour-like nodules are products of chronic inflammation, excited by the growth of organisms at certain points in the tissues. Irritation is maintained as long as the fungi grow, and as their growth is often slow, the processes are often chronic. The development of vessels is imperfect, and so degeneration is the rule. Secondary growths in other parts are due to infection from the primary focus; but organisms and not tissue-cells are the active agents.

The above diseases are as specific as the "acute specifics." Their essential lesions have a general resemblance; but the primary seats, modes of generalisation, varieties and times of degeneration, as well as the clinical symptoms, establish them as distinct diseases. The transmissibility from person to person of syphilis and glanders is well known; tubercle can be transmitted experimentally, and the clinical evidence of its ordinary communicability from man to man is very strong. Leprosy has been acquired through a post-mortem wound, and experimental inoculation has been successfully performed upon a criminal. Actinomycosis has been transmitted from man to animals. The term infective granulomata, though adopted at a time when their real nature was little understood, seems better fitted than any other to express the nature of the lesions—tumour-like bodies, consisting of granulation-tissue, and locally or generally infective.

TUBERCLE AND TUBERCULOSIS.

Tuberculosis is an infective disease, which is characterised anatomically by the formation of those small nodular lesions known as **tubercles.** The distribution of these lesions may be more or less general—**acute general tuberculosis**; or they may be limited to small areas—*e.g.*, a pleura, or the synovial membrane of a joint—**local tuberculosis**. The latter, as a rule, runs a much more chronic course than the former, and perhaps its chief danger is, that it may serve as a focus for general infection.

The virus of tubercle does not always produce nodules. Laennec divided tubercular lesions into the **nodular** and the **infiltrating.** In the latter case a diffuse inflammation is found, and microscopic examination shows the presence of numerous non-vascular collections of cells, not aggregated into visible nodules, but separated by an ordinary round-celled infiltration. The presence of the ordinary tubercles in a tissue is always accompanied by more or less inflammation, as is best seen in serous membranes.

NAKED-EYE APPEARANCES.—Tubercles are divided into two varieties, **grey** and **yellow**, the latter being later stages of the former. **Grey**, or **miliary** tubercles (**grey granulations**), are greyish, semi-translucent, rounded bodies, varying from just visible points to nodules the size of a pin's head, or larger. They are firm and shot-like, distinctly circumscribed and prominent above the surface of the

section. **Yellow** tubercles are generally larger, less regular, less closely defined and softer than the grey. They may even form masses the size of a cherry or small walnut. In some cases, most of the tubercles present are grey, whilst in others, all are yellow; but it is frequently possible, in the same case, to trace every stage in the formation of a yellow from a grey nodule. Fatty degeneration, commencing centrally, is the main cause of the difference between them. A large mass of yellow tubercle is formed, not by the growth of any single tubercle, but by the blending of several arising close together. It is often possible to recognise, round a yellow cheesy mass, a narrow gelatinous zone, consisting of grey tubercles. Grey tubercles may be also seen radiating from the cheesy focus into the surrounding tissues, thus indicating that infection from the central mass leads to the formation of fresh tubercles in its immediate neighbourhood, and these, as they enlarge and degenerate, become part of the central mass. A yellow mass thus formed is called **conglomerate tubercle.**

SEATS.—The skin and subcutaneous tissue, the mucous membranes—respiratory, alimentary, and genito-urinary—and the serous and synovial membranes are very commonly affected; so also is the pia mater. The dura mater, the ependyma, and the endocardium rarely suffer. Tubercles are frequent in the lymphatic glands, lungs, liver, spleen, kidneys, and testes; less common in the brain and spinal cord, adrenals and prostate; rare in the heart, salivary glands, and pancreas; and very rare in the mamma, ovaries, thyroid, and voluntary muscles. They are common in bone, especially in the cancellous part. They are particularly common in childhood and early adult life, but no age is exempt.

HISTOLOGY.—On examining microscopically even *the smallest tubercle visible to the naked eye,* it is found to be made up of a collection of still smaller tubercles, *each of which* as a rule contains the following elements: (1) centrally, either one or more multinucleated **giant-cells** (Figs. 131 and 132), or some granular débris surrounded by giant-cells; (2) outside the giant-cells usually, but by no means invariably, large cells with big nuclei and granular protoplasm, often called **epithelioid cells**; and (3) outside these again, a zone of **lymphoid** elements, which has no definite external or internal limit. The giant-cell or cells in many cases send off processes which anastomose

and form an open network (Fig. 133), in which the other cells, especially the epithelioid, lie. The lymphoid cells are commonly



FIG. 131.—*A Multinucleated Cell from the Lung in a Case of Chronic Phthisis.* Showing the large number of nuclei with bright nucleoli. × 400.



FIG. 132.—*A Multinucleated Cell from the Lung in a Case of Chronic Phthisis.* Showing the long branched processes, which are continuous with the reticulum of the surrounding indurated growth. Some of the processes are in connection with smaller nucleated elements. × 200.

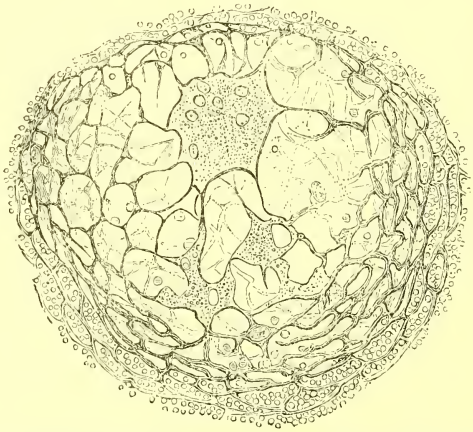


FIG. 133.—*Multinucleated and Branched Cells from a firm Grey Miliary Tubercle of the Lung in a Case of Acute Tuberculosis.* Wide meshes are seen in the immediate vicinity of the cells enclosing a few lymphoid elements. The branched processes are directly continuous with the reticulum of the tubercle. × 200.

contained in the meshes of a homogeneous or more or less fibrillated reticulum, which, in some cases, especially in slowly developed lesions, is well marked (Fig. 134). In others it is less prominent, and, according to many observers, it is not infrequently absent.

A *non-vascular* nodule of the above structure is the anatomical characteristic of tubercle, but it is not microscopically distinguishable from the products of other very local chronic inflammations. Baumgarten produced typical "tubercles" in a rabbit's cornea, by sticking fine hairs into it. Laulanié states that, in the lung-disease caused in dogs by the *strongylus vasorum*, the ova and embryos may be seen in giant-cells, surrounded by zones of epithelioid and lymphoid cells. In actinomycosis in animals an exactly similar arrangement of cells is found round about the central *actinomyces* or fungus of the disease.

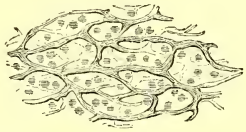


FIG. 134.—*A portion of a Grey Miliary Tubercle of the Lung.* Showing the reticulated structure often met with in these nodules. × 200.

Nor can the above structure be said to be constant. For, especially in acute cases, ending fatally, some of the tubercles seem to consist entirely of small round cells—no epithelioid or giant-cells being visible. In the lung the alveolar epithelium often enters largely into the constitution of the lesions. Tubercles visible to the naked eye will, however, generally consist of aggregations of nodules of the above structure (Fig. 102).

Source of the Cells in Tubercle.—Baumgarten's explanation is the one most generally accepted. According to him, the cells are derived from the local tissue cells, including both epithelial and connective tissue (fixed and endothelial). This observer, experimenting with albino rabbits, introduced pure cultures of tubercle bacilli into the anterior chamber of the eye. In a few days there appeared nuclear changes in the connective-tissue and endothelial cells of the iris, such as are characteristic of cell-division (p. 11). These changes were limited to the cells in which bacilli were present. They were followed by proliferation of the cells themselves, which then gradually assumed an epithelioid type. No nuclear changes, indicative of proliferation of any form of leucocytes, were observed; but the proliferating patch was gradually invaded by leucocytes, until they quite obscured the epithelioid cells. Giant-cells were occasionally present, but only in the later stages; when present, they showed no sign of division but only of degeneration.

Metchnikoff maintains that the cells, believed by Baumgarten to be the progeny of connective-tissue, are mononuclear leucocytes. In the case of the lung he admits the endothelial cells of the blood-vessels to a share in the process, and also attributes to them a phagocytic function. In his opinion, the tubercle is formed by the *accumulation, not* by the *proliferation* of phagocytes. Giant-cells, according to him are phagocytes that have combined for the common weal; while to



FIG. 135.—*A Single Tubercle*, invisible to the naked eye, from the liver of a child, aged five, who died from acute tuberculosis. A giant-cell with two groups of nuclei and several bacilli is seen near the centre. Surrounding it, is an area of commencing caseation in which the cells are becoming indistinct. Enveloping this is a zone of cells consisting of fibroblasts and leucccytes. The leucocytes are most numerous on the side where the caseation is most advanced. The whole mass is embedded among granular liver-cells in the inter-lobular area. × 250.

Baumgarten and Koch they are solitary individuals that have tried to multiply, but, though their nuclei have divided and their size has increased, have failed at the final stage of cell-division. In parts in which epithelium is present, as in the lung, liver (Fig. 135), kidney, or testicle, there can be no question but that the epithelial cells multiply freely. In a lung, affected by acute miliary tuberculosis, we find that many, even the majority, of the nodules do not possess the lymphoid structure above described, but are collections of epithelial cells in the alveoli. Giant and epithelioid cells may be present, formed apparently from alveolar epithelium, as Klein and Cheyne assert. Koch also

regards certain pigment-containing giant-cells as originating in alveolar epithelium, and quotes Cheyne's observation of giant-cells *in* the alveoli, in support of his view.

SECONDARY CHANGES.—Tubercle invariably undergoes more or less fatty metamorphosis, and **caseation** with its ultimate changes (p. 53). In some cases the nodules may become developed into an imperfect **fibroid structure**.

Caseation.—The occurrence of fatty changes and caseation, before the vessels have developed, is probably due to the action on the surrounding tissues of some substance secreted by the bacilli. This may also account for the obliteration of pre-existing blood-vessels, which accompanies the spread of the lesions. The change commences in the centre of the nodule, this being the part first developed, and consequently that which is the furthest removed from vascular supply: it is also the part at which the bacilli are at first most numerous, and it is therefore most exposed to their deadly influence. The nodule breaks down into a granular fatty débris, so that its central portions soon become opaque and yellowish (Fig. 136). In some cases the process of disintegration is rapid, whilst in others it is more gradual. It is usually most marked in the larger and more diffused lesions, and hence it is these lesions which are most commonly of a yellow colour and soft consistence ("yellow tubercle").

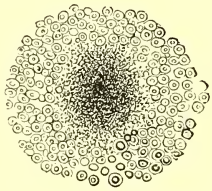


FIG. 136. — *One of the Grey Nodules from the Lung in a Case of Acute Tuberculosis*, which is becoming opaque and soft in the centre. (Diagrammatic.)

Fibroid Change.—In other cases the retrograde change is less marked. The central portion undergoes fatty degeneration and is more or less completely absorbed; whilst the ring of leucocytes, which intervenes between the bacilli and the healthy tissues, is gradually replaced by a dense, contracting, fibrous capsule. Ultimately a mere scar may remain, but points of fatty degeneration are frequent and may undergo further changes.

It will be noted that this "fibroid change" is simply the encapsulation of a slightly irritant foreign body, and might take place in exactly the same way if a bullet or piece of wire lay in the tissues instead of tubercular organisms in fatty detritus. This replacement of the tubercular tissue by scar-tissue occurs in the smaller lesions and in many of larger size which open upon the inner or outer surface of the

body, and from which the infective material can be thus discharged. The change obviously tends to protect the organism against generalisation from the focus in which it occurs, and indicates that the tissues have gained the upper hand — they have imprisoned the bacilli. There is the same antagonism between the organisms and the tissues in tubercle as in other diseases, and the resisting power of the tissues may also be sufficient to enable them in the long run to overcome the invaders—a fact for some time overlooked. But frequently the predisposition of the tissues to suffer from tubercle is so great, or the dose of the organisms is so large—as when most of the contents of a small cavity which had just burst into a bronchus is sucked by inspiration into other air-tubes—that a widespread, diffuse inflammation results; and the more extended the lesion, the more rapidly and freely the inflammatory products caseate.

Sometimes, especially in cases which have run a chronic course, and in which the diagnosis may have been "chronic bronchitis," hard, glassy bodies, often specked with black pigment, are found in the lung-tissue. There is no caseation, and the microscope shows the masses to consist of almost hyaline fibrous tissue. This complete fibroid transformation is said by Birch-Hirschfeld to occur occasionally in lymphatic glands, and is often thought to indicate that the bacilli are dead. On the other hand, while the caseated material persists, the focus remains infective, and the organisms or their spores, though quiescent, are alive.

Calcification frequently ensues upon caseation, when the cheesy products become encapsuled, and almost all fluid is absorbed: the deposit of earthy salts in this truly cheese-like material converts it either into a gritty mass or into a more or less irregular stony body. Caseous mesenteric glands are especially prone to this infiltration.

Sections of these calcareous nodules, when decalcified and examined under the microscope, are seen to consist chiefly of a series of concentric layers. These layers are composed of a substance which, according to Metchnikoff, gives the same reactions as that forming the envelopes of the tubercle bacilli. Arguing from his experiments on Algerian rats, he maintains that these layers are formed by successive secretions of the bacilli, and that they subsequently become infiltrated with phosphate of calcium. According to his view, the concentric layers would seem to be the lines of defence which the bacilli throw up against the advancing phagocytes, while the calcification is the investing earthwork by which the attacking phagocytes seek

to enclose, and to reduce by starvation, the organisms they cannot reach, or reaching, cannot destroy.

Softening and Chronic Abscess.—Caseous masses do not always dry up and become encapsuled, but often soften and break down into the pus of a chronic abscess; and even when they have become encapsuled and calcified, softening may occur round about them: a chronic abscess is then formed, and the dead material is discharged. It is the smaller encapsuled foci, and especially those which lie deep in the substance of organs, that become dry and calcified; whilst the extensive, diffuse lesions, and those lying near a skin or mucous surface, tend to soften. In other words, the less the resistance of the tissues to the infective process, or the greater their proneness to be irritated by the tubercular organism, the greater is the tendency to softening. It seems likely that this irritation of the tissues is the cause of the exudation of fluid into the cheesy mass, and that this exudation changes the latter into a chronic abscess; for an examination of the "pus" of a chronic abscess shows that it consists chiefly of fatty granules suspended in fluid, with here and there a fattily degenerated, granular leucocyte. The fluid, therefore, is quite different microscopically from that of an acute abscess (p. 283). It differs also to the naked eye, being generally whiter and thinner than true pus, while it often contains curdy masses, which may be either gritty or stony from calcification. The "pus" of chronic abscess, being thus formed by the suspension in an albuminous fluid of fatty particles derived from the fatty degeneration of cells, has received the name of "pathological milk." The enormous majority of chronic abscesses are of tubercular origin: a tubercle forms, spreads and softens as above described—the originally firm swelling becoming more and more fluctuating as the softening proceeds. So chronic is the process that there is often no sign of inflammation until just before the "abscess" bursts, when the tense skin, where it is pointing, becomes red, shiny, and progressively thinner. Ultimately the epidermis bursts, and the cavity discharges its contents. The wall of such a cavity is lined by a thick layer of pale purplish granulation-tissue, in which are yellow foci. This lining is so loosely adherent to the surrounding tissues that scraping with a sharp spoon easily detaches it, and brings it away either entire or in large pieces. The tissues beyond it are not infiltrated. It is very important that the wall should be removed from such abscesses, as well as the base from any ulcers resulting from their bursting; for the granulation-tissue is infected by the tubercle bacilli, and will

continue to caseate and soften in spots, and perhaps slowly to invade surrounding parts. Healing is impossible until the diseased layer has been cast off, and replaced by healthy granulation-tissue.

This account of the formation of a chronic abscess holds good wherever it may appear: in the subcutaneous tissue (*subcutaneous strumous nodule*, so common in children); in a lymphatic gland (the *strumous abscess par excellence*); in the lung, where sooner or later it bursts into a bronchus, discharges its contents, and forms a *cavity* or *vomica;* in the thickened synovial membrane of a scrofulous joint (*white swelling*); or in a bone, as is seen in caries of the spine. The chronic abscesses which arise in connection with deep bones, especially those of the spine, are frequently called *gravitation abscesses*, because the pus often runs long distances among the soft parts before it reaches the surface, and usually in a direction towards the feet. But extension by no means always occurs in this direction, and, when it does occur, is not arrested by placing the patient in the horizontal position. We may therefore conclude that in these, as in all other cases, the pus spreads in the direction of least resistance, and that gravity has comparatively little to do with it. Instances have been recorded of abscess starting from the lower dorsal or lumbar spine, entering the sheath of the psoas, causing gradual absorption of its muscular fibres, working its way beneath Poupart's ligament, taking the course of the profunda artery, passing through the adductor magnus into the popliteal space, penetrating between the superficial and deep posterior leg-muscles, and finally pointing by the inner malleolus. Such an abscess is contained in a dense fibrous sheath, formed by inflammatory thickening of the natural connective-tissue. This sheath is sometimes strong enough to be dissected out and dried. The cavity is crossed by stoutish bands, many of which contain vessels, and care must be taken lest a finger introduced during life tear them. The inner surface of the cavity is but slightly vascular—the contrast between the chronic and acute abscess in this respect being very marked. It is usually coated with a cheesy deposit of irregular thickness, beneath which lies a very thin layer of granulation-tissue. At the upper extremity is the diseased bone—the *fons et origo malorum.*

In the pus of these abscesses, no organisms can be discovered by the means at present in use, yet the pus is infective and produces general tuberculosis when injected into animals.

RESULTS.—Recovery may occur after the discharge or complete

removal of all tubercular tissue. Under these circumstances, healthy granulation-tissue springs up and develops into a **scar**, filling up and drawing together the cavity of the abscess or ulcer. There is always loss of substance.

In the condition known as **obsolescence**, the caseous focus is surrounded by a dense fibrous capsule, often with radiating bands passing from it into the surrounding tissues. It is often seen at the apices of lungs, and may serve as a practical cure; but, theoretically, it is not one unless the tubercular organisms are dead, for they may at any time be carried from the focus into the system at large.

Lastly, **death** frequently results from tubercular processes, both general and local. The acute general tuberculoses, affecting chiefly meninges, lungs, and peritoneum, kill by their general toxic effect, by fever, and by interference with the functions of vital parts—*e.g.*, the functions of essential cerebral centres may be arrested by the compression of the effusion. Chronic local tuberculoses kill, either by leading to a general outbreak, or by exhaustion from fever, pain, and profuse and prolonged discharge—especially when septic processes are superadded (p. 328). Indirectly, a tubercular process may open the door to some infective wound-disease such as erysipelas or pyæmia.

ÆTIOLOGY AND GENERAL PATHOLOGY.—In 1857, Buhl, commenting on the very frequent presence of caseous foci in general tuberculosis, and on the local infection which often occurs round such foci, promulgated the view that a poison, capable of giving rise to tuberculosis, was generated during the caseation of inflammatory products. *Caseation* was the one essential feature. Virchow, however, pointed out that caseation occurred in new growths and under circumstances in which all connection with tubercle could be negatived.

In 1865, Villemin made numerous experiments, which seemed to demonstrate the infective nature of tuberculosis. He placed tubercular material beneath the skin of rodents, and general tubercle developed. Villemin believed, therefore, that tuberculosis was a disease due to a specific poison contained in the foci of the disease. His experiments were repeated by Cohnheim and Fränkel, Wilson Fox, Sanderson and others, who found that tuberculosis followed the inoculation of cheesy material which was presumably not tubercular, and even such simple inflammation as resulted from the insertion of setons, of vaccine virus, and bits of cork or paper. Sanderson, how-

ever, concluded that nothing induced tuberculosis *with such certainty* as material taken from an undoubtedly tubercular source.

Klebs pointed out that possibly the non-tubercular material might have become contaminated by the tubercular virus, as at that date precautions were not very stringent. It was probable, too, that in many cases, where septic materials were used, the process induced was pyæmic.

It then occurred to Cohnheim and Salomonsen to select the anterior chamber of the rabbit's eye as the point of inoculation. Here the results of the inoculation could be watched from day to day, and as primary spontaneous tuberculosis of the iris had never been seen in rabbits, the possibility of this could be excluded. It was thus proved that, whilst inoculation of *non-tubercular* material into the anterior chamber of the eye invariably failed to induce tuberculosis, the inoculation of *tubercular* material produced tubercles in the iris and, a little later, in the body at large. The proof of the infective nature of the tubercular process was thus completed, and it was further shown that tubercular materials, from widely different sources, contained the same virus. Tappeiner caused dogs to inhale, daily for fourteen days, six grammes of tubercular sputa delivered during six hours from a spray into a narrow box containing the animal: all became tuberculous, the twenty-third day being the earliest upon which tubercles were found. Thus tubercle came to be regarded as a *specific infectious disease*.

Many of those who held this belief suspected that the virus was a vegetable parasite and searched for it. Between 1877 and 1882 several premature announcements were made.

The next publication was Koch's paper.* By a special process of staining he first demonstrated the constant presence of peculiar bacilli in eleven cases of acute tuberculosis, twelve cases of cheesy broncho-pneumonia, one of tubercular nodule in the brain, and two of intestinal tuberculosis in man. Ten cases of perlsucht, and cases of spontaneous tubercle in monkeys and other animals were investigated with a like result; and finally the bacilli were found in a large number of rodents and five cats artificially infected. As proving that the tuberculosis resulted from the inoculation and was not accidental, there was (1) the invariable coincidence; (2) the more rapid development of the

* "D. Ætiologie d. Tuberculose:" *Berl. klin. Wochschr.*, No. 15, 1882. His paper on the same subject in the *Mittheil. aus dem Gesundheitsamte*, vol. ii. 1884, translated in the New Sydenham Society's "Microparasites in Disease," is fuller, and should be read by all.

artificial than of the spontaneous tuberculosis; (3) the early infection of the glands nearest the seat of inoculation, whereas the bronchial glands usually enlarge first in spontaneous disease; and (4) control-experiments in which animals were treated exactly as the inoculated animals were, with the single exception that no *living* bacilli were introduced: in these no tuberculosis occurred.

Finally, the bacilli were cultivated at 98° F. to 100·4° F. (37° to 38° C.) in sterilised blood-serum. After thus passing through many generations, these bacilli were suspended in distilled water and injected: they then produced tuberculosis as surely as did the original material.

These results have since been fully confirmed, and their truth is now

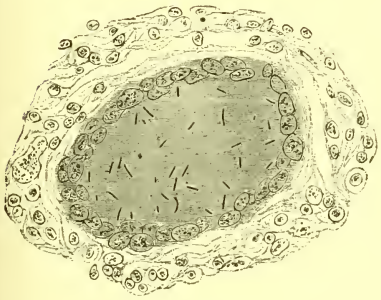


FIG. 137.—*Tubercle Bacilli in Giant-Cell.* From tuberculosis of horse. × 600. (Cheyne.)

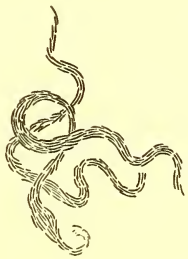


FIG. 138.—*Tubercle Bacilli*, from a colony on blood-serum, showing the wavy parallel lines. × 500. (After Koch.)

unquestioned. We are therefore justified in believing that the bacillus tuberculosis is the cause of all tubercular processes. Its presence, rather than any anatomical structure, is, at least in the early stages, the essential characteristic of tubercle.

Characteristics of the Bacillus.—The bacillus is 2 to 6 μ long, two or three, placed end to end, making up the diameter of a red blood corpuscle. It is very thin ($\frac{1}{5}$ to $\frac{1}{6}$ of length), motionless, and rounded at the ends. It can be stained with Ziehl's fluid (p. 331), or by Gram's method (p. 330). It has generally a beaded appearance—clear spots (4 to 8) alternating with stained parts. The bacilli are usually straight, but may be curved; they occur singly, but sometimes in pairs. Multiplication is very slow and takes place by fission and possibly by spore-formation, though this is uncertain. As a rule, the bacilli are found in the cells of the tubercle, especially in

giant-cells opposite to the nuclei. They are well shown in the accompanying drawing (Fig. 137).

The organisms can be cultivated on media containing glycerine or blood-serum. They are aërobic, but as they grow only at high temperatures 82° F. to 108° F., they probably do not multiply outside the body, but live a wholly parasitic life. To the naked eye (see Frontispiece), the colonies have a heaped up, scaly appearance. When examined under the microscope, the margins of the colonies show a peculiar wavy form due to parallel chains of organisms following the same curve (Fig. 138). Although the bacilli do not *multiply* outside the body, they can *live* for a long time, having been found to retain their virulence after existence for forty-three days in putrid sputum, and for one hundred and eighty-six in the dry state. In putrid fluids they do not long hold their own against the rapidly multiplying septic organisms, which are specially adapted for the ordinary conditions external to the body. It is in the state of "dust" that we are most likely to meet with tubercle bacilli in our surroundings, and obviously this is the state in which they are most fit to cause a fresh infection.

With regard to the **origin of the tubercle bacillus** from some non-pathogenic form, no other bacterium, even under such favourable conditions as the bodies of rabbits and guinea-pigs present, has been found to develop any of the peculiarities of the tubercular organism. Nor are there at present any facts known as to circumstances under which its virulence can be modified—increased or attenuated. Nearly two years' cultivation external to the body caused no change in the latter direction (Koch). We must conclude, therefore, that these tubercle bacilli multiply only in the body of man or some other animal, and that, consequently, the bacilli which cause a fresh infection come either directly or indirectly from some tubercular individual.

Obviously, all cases of tubercular disease in man are not equally prone to **disseminate the bacilli**. These may be eliminated with the sputum, the fæces, the urine (in tuberculosis of the genito-urinary tract), and discharges from tubercular ulcers and abscesses, but the first is the only common source of infection. When we consider that about one-seventh of mankind die of phthisis, and that in all cases in which cavities form, the patients for weeks or months are expectorating large quantities of bacilli, we see that this one source is capable of keeping up an ample supply. The bacilli expelled by cough with small particles of mucus may be directly inhaled by the healthy; but

sputum, which dries upon handkerchiefs, bedclothes, and woollen garments, thence to be detached as dust, appears to be the most fertile source of infection. Bacilli found in the air are usually adherent to some bit of vegetable fibre, hair, or epidermis.

Tubercular disease in animals is also a frequent source of infection to man. It is true that they produce no sputum, that few or no bacilli are expelled from their lungs, and that bacilli are not frequent in their excreta; but the *milk of tubercular animals* may give rise to infection. As it contains bacilli only when the mammæ are tubercular, this cause is easily preventible, if dairies are efficiently inspected. Lastly, there is another possibility of infection through the ingestion of *tubercular meat*. This can undoubtedly occur, as has been proved by feeding animals on tubercular flesh; but many things militate against its occurrence in adults, in whom primary intestinal tuberculosis is not at all common. The flesh, if visibly diseased, is usually rejected; it is generally raised above 100° C. before being eaten; the disease in animals used for food, and especially in cattle, is usually localised, and infection could follow only upon eating the tubercular parts, such as the lungs, or glands. While, therefore, the domestic animals are possible sources of infection, in the majority of cases the disease is conveyed from man to man.

The bacilli are readily destroyed by boiling, by sunlight, by perchloride of mercury solution, and by carbolic acid; but they resist the action of a 1 per 1000 solution of the perchloride for some minutes. A five per cent. solution of carbolic acid acts more rapidly. Desiccation without sunlight does not destroy them.

Modes of Entry of the Bacillus into the Body.—The sound **skin** would seem to be impassable, and but a few cases have been recorded in which *infection through wounds* has occurred. One of the most conclusive is the following: A perfectly healthy woman, with no tubercular history, cut her finger with a broken vessel containing sputum swarming with bacilli. Acute inflammatory symptoms followed, but subsided under carbolic fomentation. In the meanwhile a small subcutaneous nodule of granulation-tissue developed and was removed at the end of a month, the wound healing by first intention. Then came pain in bending the finger, a swelling extending along the tendon into the palm, and swollen glands—two above the elbow and two in the axilla. All these parts were completely removed, the wounds healed at once, and no further spread took place. The tendon-sheath was full of granulation-tissue containing numerous tubercles;

the glands were simply hyperplastic. Bacilli were fairly common in both. Several observers have stated that dissecting warts are tubercular, because they have constantly found tubercle bacilli in giant-cells taken from degenerating nodules in the affected skin. Moreover these warts have commonly arisen after contact with tubercular subjects. Riehl and Paltauf regard the warty, inflamed papillæ as resulting from a mixed infection, cocci having been inoculated with the bacilli. Volkmann examined one case of scrofulous eczema, and discovered the bacillus of tubercle in the epithelial and other cells. He therefore believes that these catarrhs of the skin, and the more frequent catarrhs of mucous membranes, are due to the irritation of this organism. Certainly lesions of this kind lead to the development of strumous glands; and, in order to account for the apparently primary enlargement of superficial glands, Koch put forward the now generally accepted view, that the swelling has really been preceded by some scratch or slight sore (on the skin, whence lymphatics pass to the gland) upon which tubercular bacilli have fallen, and whence they have been conveyed into the lymphatics too speedily to interfere much with healing. Lastly, tuberculosis is said to have been conveyed by *vaccination*. The evidence is of the usual *post hoc* kind, and the statement has probability against it, for the *blood* of tubercular animals is only infective in the most acute cases of general tuberculosis; and the children from whom the "lymph" was taken were probably, to all appearances, healthy.

Lupus is possibly another illustration of tubercular infection of the skin (p. 419).

The **mucous membranes**—pulmonary and digestive—must therefore ordinarily afford passage to the bacilli: the possibility of this has been demonstrated by the success of *inhalation experiments* with tubercular sputa and cultivations, and of *feeding experiments* with tubercular tissues. Pulmonary tuberculosis being much more frequent than intestinal, we may assume that bacilli more often pass into the tissues through the pulmonary than through the alimentary mucosa. The difficulties in both cases are considerable. As regards the thorax, the bacilli are drawn most deeply into the lungs by deep inspirations through the *open mouth*. Evidently they cannot be carried beyond the regions of the tidal and complemental air, and will therefore be deposited in the smaller bronchi; but they multiply so slowly that they are usually expelled by ciliary action and coughing before they can seriously injure any spot and effect an entrance. To enable them to

do this, specially favourable circumstances are necessary, such as the removal of much of the bronchial epithelium (after measles); the presence of bronchitis, with tenacious, and therefore retained, secretion; and the existence of pleural adhesions or of a badly formed thorax, preventing full expansion of the lung, and therefore leading to local retention of secretions. Primary intestinal tuberculosis (which would occur from tubercular food) is rare, except in children; but ulceration of the bowels occurs once in every three cases of phthisis, being apparently due to infection by the bacilli in swallowed sputum. Koch says that the intestinal mucosa offers a less favourable point of attack than the pulmonary; that the adult bacilli, like anthrax bacilli, are usually destroyed in the stomach, whilst the spores escape—so only spore-bearing bacilli can infect the bowel, and these only on condition that they are not hurried through the canal. Lastly, it seems that, just as a superficial gland may be infected from some lesion of the skin so slight as to escape notice and to leave no trace, so the bronchial and mesenteric glands may be infected by bacilli which pass through their respective mucosæ without leaving any permanent trace of their passage. Instead of settling in the pulmonary or intestinal tissue, they are evidently carried on by the lymph-stream and, in the majority of cases, arrested in the *nearest* gland, though the arrangements of lymphatics is such that they may be at once conveyed to more distant parts. The affected glands enlarge, caseate, and often infect others. Such caseous glands act as reservoirs of bacilli and their spores, and too often prove sources of more or less widespread infection.

It is well known that in young children the *lungs* are not affected in the same proportion as they are in later life, that the disease is not so localised, and that the lymphatic glands especially are more universally affected. The intestine seems in a large number of cases to be the part primarily attacked (p. 408), even, as Woodhead insists, in those cases in which patients ultimately succumb from disease of the lung. Thus we can often trace the infection from an old calcified gland in the mesentery to the retro-peritoneal, posterior mediastinal, and bronchial glands, and thence to the lungs; in which organs the disease radiates from the root.

Having no power of locomotion, the tubercle bacilli must be carried through the pulmonary mucosa by leucocytes like carbon particles. The leucocytes, wandering short distances from the lymphoid tissue, may easily reach the surface and there meet, enclose, and carry back

bacilli. If the cells sicken while the bacilli survive, the latter may find themselves in some place where they can thrive and multiply, and thus tubercles may arise. In catarrhal states more phagocytes will reach the inflamed surface, and more bacilli are therefore likely to be introduced into the tissue.

A somewhat strained analogy may be drawn between the collections of lymphoid tissue distributed along the mucous surfaces and the fortified towns which guard a frontier. The lymphoid masses serve as garrisons from which leucocytes issue out and deal with any organisms they may chance to meet. Unfortunately the discriminating power of the phagocytes is not equal to the occasion, and they sometimes carry back bacilli whose subsequent development reminds one of the old story of the Trojan Horse.

Predisposition.—Nothing is more certain than that individuals vary in their liability to tubercular diseases; for these are far commoner in the young than in the old, and run markedly in families. We have no knowledge of what constitutes this predisposition, which may be inherited or acquired, local or general. A small flat chest and a tendency to catarrh are often present in people who ultimately develop phthisis, and the absence of free respiratory movements is often held to favour the entry of the bacilli. Often, too, members of tubercular families are specially exposed to infection in nursing a sick relative. But even allowing for these facts, it seems impossible to believe that there is no difference between the predisposed and the immune, save that in the latter the bacilli do not gain entrance; for it is so much more probable that in many cases they enter but fail to grow, being destroyed by the tissues. How can we explain acute meningeal tuberculosis, or tuberculosis limited to the peritoneum, in both of which multitudes of bacilli must have been thrown into the circulation from some bronchial gland or other focus, unless we assume that the bacilli could not develop elsewhere than in the meninges or peritoneum respectively?* How, too, should we otherwise explain the recovery of some people from phthisis, except by assuming that the soil, which was at one time favourable to the growth of the bacillus, became later on unfavourable? The predisposition seems to vary from time to time in the life of the same individual.

* It is possible that a single infection of the pleura, pericardium, or peritoneum might be spread more or less rapidly over the whole membrane through its lymphatics and by means of the movements of the organs. It is difficult to conceive an infection of both Sylvian arteries and spread against the lymph stream, from the base to the convexity of the brain.

Development in the Tissues.—Having found a spot at which it can grow, the bacillus proceeds to multiply: most bacilli are taken up by cells which enlarge into giant-cells and become the centres of typical "tubercles" (p. 385). The presence of these in a tissue excites more or less inflammation, often so much that we find the tissues diffusely infiltrated, distinct nodules being scarce or absent (*infiltrating variety*). Caseation at the non-vascular centres soon follows, being preceded by coagulative necrosis of the cells—due, no doubt, to the direct action of the products of the bacilli. The nearest lymphatic glands often become affected. The primary lesion may become localised, as before explained (p. 389), or it may act as a starting-point for fresh infection.

Modes of Spread.—(1) **By Continuity of Tissue, and by Lymphatics.**—This is the way in which the masses of conglomerate yellow tubercle are formed, and in which patches of infiltrating tubercle—such as of the skin, *scrofulo-derma*—spread. It is supposed that leucocytes enter the primary focus, take up a bacillus or a spore, and wander out again along fine lymphatics into the surrounding tissues, there to sicken and swell into a giant-cell not far from the parent mass. A fresh tubercle thus forms and caseates, and its margin coalesces with that of the parent mass, which in this way gradually enlarges. The young tubercles form the greyish translucent ring round the conglomerate mass (p. 385), with here and there an off-shoot of slight length. But, occasionally, a leucocyte, containing a bacillus, finds its way into a lymphatic, and is carried by the lymph-stream to the nearest gland. The situation being a favourable one for observation, the process of infection of mesenteric glands from an intestinal ulcer may sometimes be traced by tubercles along the track. Ponfick has described tubercles in the thoracic duct in cases of acute tuberculosis: this he regards as evidence that the bacilli had passed by this channel to the blood.*

(2) **By Infection of one part from another.**—Examples of this are easily found. Perhaps the best is seen when a sudden inspiration follows the bursting of a tubercular focus into a bronchus, and draws the infective material into many other bronchi, with the result that a caseous pneumonia develops, beginning in numerous patches of

* The lymphoid tissue is not only the medium by which the disease spreads, it is also the place where the tubercle bacilli are most actively attacked, and where therefore they are most likely to be destroyed. If the organisms pass the lymphoid tissue in the mucous membrane, they have still to deal with the lymphatic glands beyond.

"racemose tubercle"—*i.e.*, the tubercular tissue is moulded into racemose forms by the alveoli in which it grows. Other examples are the infection of the palate from the tongue, of the intestine from swallowed sputum, and of the lower urinary tract from the kidney.

(3) **By Veins.**—Müggе described tubercular infiltration of the walls of pulmonary vessels, especially veins, in pulmonary tuberculosis; and Weigert believes that this actual growth of the bacillus into the circulation is frequently the source of general infection.

(4) **By Arteries.**—In two cases of death from acute tuberculosis examined respectively by Koch and Cheyne, there were present caseated bronchial glands. In each case a *pervious artery* was found *with its wall infiltrated with tubercle.* This was the assigned origin of the general infection.

In one or more of these different ways, the virus reaches the blood and is carried all over the body, developing when and where the conditions are suitable—in the lungs, meninges, joints or other parts. If the supply of virus is plentiful, the case is likely to be acute. Laennec used to teach that the tubercles appeared in crops, distinguished by the amount of degeneration they had undergone. This would indicate an intermittent supply.

Generalisation.—An acute miliary tuberculosis of the meninges, lungs, peritoneum, and various abdominal viscera plainly implies that a large number of bacilli have found their way within a short space of time into the blood: the result is just such as follows the intravenous injection, in rodents, of a syringeful of a pure cultivation of the bacilli. As it is inconceivable that bacilli in such numbers could be absorbed so rapidly through a mucous membrane into the blood, it is necessary to assume the existence of some primary focus, where bacilli have multiplied, and whence they can be poured into the blood-stream. The pulmonary mucous membrane being that through which bacilli commonly enter the system, it follows that the focus in which this multiplication occurs, and whence generalisation usually takes place, is a caseous bronchial gland; though generally there is evidence of tubercular disease of one or both lungs as well. But acute miliary tuberculosis may spread from any localised focus containing living bacilli. Extension by means of any lymphatic vessel leads to the formation of tubercles along this vessel, or in glands through which the lymph passes. If the thoracic, or right lymphatic, duct be affected, the organisms may also find their way into the systemic veins. They would next reach the lungs; and the bacilli are so small that they

would easily pass through the pulmonary capillaries into those of the systemic circulation.

Limited Infection. — We have spoken of *acute general miliary* tuberculosis, using the term in contra-distinction to a *localised* tuberculosis—*e.g.*, a mass of conglomerate tubercle in the brain, or a caseous gland. But even a "general" tuberculosis, due apparently to the rapid entrance of numbers of organisms into the blood, is far from being really general; for while the lungs, spleen, and liver are very frequently affected, the voluntary muscles and mammæ (p. 385) nearly always escape. Thus we have a series of regular gradations commencing with the most widespread miliary tuberculosis, and including successively cases of miliary tuberculosis limited to the meninges or peritoneum; cases of multiple infiltrated tuberculoses—*i.e.*, tubercle limited to glands, skin, or bones and joints; and finally cases in which a single spot of skin, a single joint, or a single gland seems to be affected.

As we have before said (p. 400), the selection of special organs in "general" tuberculosis seems to indicate special **predisposition** on the part of these organs. There is no reason for assuming that the bacilli are arrested in them rather than in other parts. The same explanation would appear applicable to cases of limited miliary tuberculosis, and may possibly be the reason why tubercular meningitis affects the base, rather than the convexity, of the brain. Again, there seems no other explanation to offer of what seems to be a well-established clinical fact—viz., that children who suffer from multiple lesions of skin, glands, bones and joints do not develop visceral tuberculosis nearly so often as those in whom a single joint is affected.

Next, with regard to the **dose of organisms**: this may be large or small. It may be single, or it may be repeated at longer or shorter intervals. The different doses may come from the same or from different foci, giving rise to the successive "crops" of tubercles to which Laennec drew attention—the more recent being small and grey, and the older large and yellow. When only a few bacilli enter the circulation at one time, the infiltrations which they excite reach a far larger size than they could possibly attain in the speedily fatal general cases. Many of the cases in which single glands are affected are doubtless due to infection from small wounds or tubercular sores, either of the skin or of the mucous membrane from which they obtain their lymph-supply. But many cases of localised tuberculosis,

especially of bone and joint, admit of no such explanation: these Koch believes to be due to the entry into the circulation, and lodgment in the affected part, of a single bacillus, and he thinks that in these cases—as in those of widespread infection—the organism is obtained from some primary focus, usually a bronchial gland, whence it has, as it were accidentally, slipped by the lymph-path into the blood. He thinks it highly improbable that even a single organism could pass into a capillary of the lung from an alveolus without causing a tubercular focus in the lung itself.

The **seat of infection** may not be without effect in explaining some peculiarities of the disease, and should be borne in mind. As to **heredity**, tubercle, unlike syphilis, very rarely extends in utero from the parent to the fœtus: Koch found that guinea-pigs pregnant at the time of infection, or becoming pregnant soon after, did not transmit the disease to their young.

It is impossible to explain why some tubercular processes remain local, whilst others generalise. Blocking of lymphatics, non-invasion of the walls of blood-vessels, feeble local growth of the bacillus, healthy resistance on the part of the tissues in general, may afford hypothetical explanations.

Although in the great majority of cases of acute tuberculosis, a primary cheesy focus is found, it must be remembered that *caseation, per se,* has nothing whatever to do with the *production* of the tubercular virus.

Tuberculosis of the Pia Mater and Brain.

Tubercular Meningitis.—In the pia mater the tuberculous process is associated with inflammation of the meninges and superficial parts of the brain, constituting the condition known as **tubercular meningitis** (really meningo-encephalitis). This is almost invariably a part of a general tuberculosis.

The process is almost exclusively confined to the pia mater at the base of the brain, and the *grey tubercles*—which may easily escape observation—are seen in connection with the small arteries in the Sylvian fissures, and are deeply seated between the convolutions. A few scattered granulations are frequently visible on the upper surface of the hemispheres. (To see the tubercles, strip off a piece of membrane, with a Sylvian artery and its branches, float it in water and spread it out on a glass plate; examine over a dark background.)

The inflammatory growth originates in the perivascular lymphatic sheaths which enclose the small arteries of the pia mater (Fig. 139); and, by a double process of proliferation and (p. 387) infiltration, commencing at several centres, numerous small grey nodules are produced around the vessel. These, which are distinctly visible to the naked eye, cause an external bulging of the sheath, and a diminution in the calibre, or even complete obliteration, of the enclosed vessel.

The localised obstructions to the circulation, which result from the pressure of the perivascular nodules, increase the hyperæmia at the

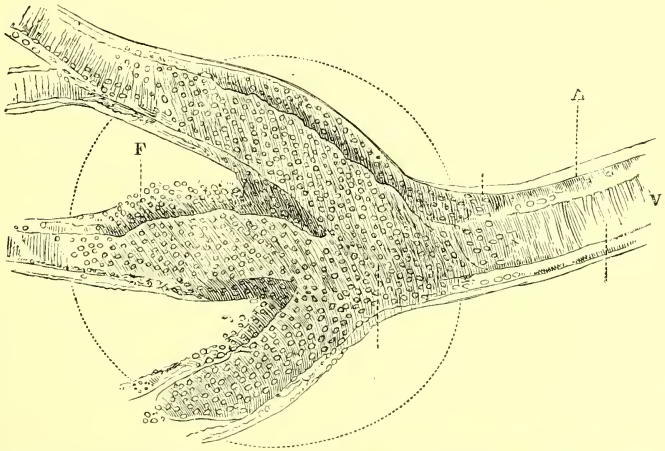


FIG. 139.—*Miliary Tubercle in the Pia Mater.* The dotted line indicates the original size of the tubercular nodule. A. The lymphatic sheath. V. The blood-vessel. F. Elements within the sheath. × 100. (Cornil and Ranvier.)

base of the brain, which thus becomes exceedingly vascular, there being in some cases rupture of the vessels and extravasation of blood. A *fibrinous transudation* takes place from the hyperæmic and injured vessels; blood-corpuscles escape; and thus the meshes of the pia mater become infiltrated with a sero-fibrinous or puriform liquid, which tends to collect in the grooves between the convolutions. The subarachnoid fluid is turbid and increased in quantity: pressure within the dura mater rises steadily.

These changes in the pia mater at the base of the brain are attended by hyperæmia, infiltration with leucocytes and fluid, and softening of the subjacent cortical substance, accounting for the early delirium and

hypersensitiveness of the special senses. The ependyma and choroid plexus also become exceedingly vascular, while the *walls of the ventricles*, the *fornix* and the *soft commissure, soften.* The *lateral ventricles* become progressively *distended* with fluid (*acute hydrocephalus*), so that the *convolutions* on the surface of the hemispheres are found pressed against the skull and *flattened.* It is uncertain how far this fluid is due to local inflammatory exudation, and how far to dropsy. The exudation generally causes marked pressure upon the veins of Galen near their entry into the straight sinus. All trace of fluid is driven from the subdural space and the *arachnoid* is dry and *sticky.*

The insensibility, deepening into coma which precedes death, is accounted for by the rise in intracranial pressure, and by the injury to the cells of the cerebral centres which results from the inflammatory process and the prolonged high pressure to which they are subjected.

Tuberculous Masses in the Brain.—Large masses of conglomerate tubercle (p. 385) are occasionally met with in the brain, unassociated with any general tuberculous process, yet, curiously, in spite of their considerable size, they rarely give rise to symptoms indicative of pressure. The explanation is that their growth is very slow, and other cells assume the functions of those destroyed, whilst fresh conducting paths are opened up—compensation being thus effected. The masses, which vary in size from a hazel-nut to a hen's egg, commonly occur in the cerebral substance, especially at the base of the brain. They are of a pale yellow colour and firm consistence, and usually form round globular tumours. Their surface is often seen to be covered with minute grey nodules, which extend into the surrounding tissue; and, on section, similar nodules are sometimes visible, scattered through the substance of the tumour. In most cases only one or two such masses are found, but occasionally they are more numerous. They occur especially in childhood. Near the edge, where the structure of the tubercles is recognisable and typical (p. 385), compressed or obliterated blood-vessels may be seen. Attention has already been drawn to the infective nature (p. 401) of these masses.

Tuberculosis of Lymphatic Glands.

In the lymphatic glands, tuberculous processes give rise, in the first place, to changes in the cortical portions of the gland, inasmuch as it is with these that the infective material, which is brought by the

lymphatic vessels, first comes into contact (Fig. 140). In the earlier stage of the process small pale grey nodules are often visible. These are scattered through the warmer-coloured, vascular cortex. They gradually increase in size and become caseous. The gland meanwhile enlarges from the addition to its substance of these "tubercles," which gradually spread in along the lymph-sinuses to the medullary portion.



FIG. 140.—*Tuberculosis of a Lymphatic Gland.* The earliest stage of the process, showing the giant-cell. × 200.

By this time the distinction between the medullary and cortical portions is lost, in consequence of the infiltration and filling up of the lymph-sinus. On section at this stage the gland presents a greyish homogeneous surface, on which are blotches of caseous material. Fibroid changes frequently follow and the capsule thickens, so that the caseous masses become surrounded by dense fibroid tissue. The whole gland may be ultimately converted into a caseous mass. The caseous portions may subsequently soften, dry up, or calcify (p. 389).

Sometimes no "tubercles" are visible, and a section in the early stage has a pulpy, swollen appearance, and may be distinctly more vascular than normal: microscopically, a round-celled infiltration, with a few large cells, is found. The result of the infection has been a more acute and diffuse inflammation than that above described. Caseous patches and fibroid changes ultimately appear.

As before stated, the affection of lymphatic glands is in most cases secondary to a tubercular inflammation in the area whence they draw their lymph; but sometimes it *appears* to be primary, bacilli having entered through mucous membrane or skin without exciting any marked inflammation. The glands most commonly affected are the bronchial, mesenteric, and cervical.

Tuberculosis of Mucous Membranes.

The alimentary, genito-urinary, and respiratory mucous membranes may all be seats of tubercular infiltration and ulceration: it is extremely probable that some catarrhal affections of the tonsils and pharynx, of the Eustachian tube and middle ear, as well

as of the intestine, are due to the irritation of the tubercular organism.

Tubercular ulceration or fissure of the lip, usually with marked thickening, is not uncommon in children and young adults. On the tongue and pharynx, tubercular ulceration is rare, and is usually secondary—at least in point of time—to phthisis. The occurrence of tubercles in the œsophagus and stomach is very rare, but cases have been described. The course and the microscopic and naked-eye anatomy of all these ulcers is the same. They will therefore be described under the heading of "Intestine," in which part of the alimentary tract they are most frequently found.

Intestine.—Primary tuberculosis of the intestine is rare in adults. It is probably caused by infection from tubercular milk or meat. Secondary infection of the intestine occurs in from half to two-thirds of the fatal cases of phthisis, and is caused by swallowed tubercular sputum. The small and the large intestine are said to be affected with about equal frequency, and *both* are generally involved. The morbid process begins in the solitary and agminated follicles, and is most marked where these are most numerous, namely, at the lower end of the ileum and in the cæcum; but any part may be affected (p. 399).

The first stage of the process consists in the appearance of tubercles in some solitary glands and in certain follicles (*not* all) of some Peyer's patches. The affected lymphoid tissue swells, and therefore projects too much above the surface of the membrane. The new elements, consisting largely of leucocytes, then undergo fatty changes and soften. The degeneration in Peyer's patches, commencing at a number of separate centres, is followed by a patchy ulceration of the mucous membrane; and the process extends by the appearance and subsequent breaking-down of fresh tubercles at the margin, until a considerable part of the patch is destroyed. As the result of these changes an ulcerated surface is produced, the floor and edges of which are more or less thickened, owing to the production of tubercles and tubercular infiltration in the surrounding tissues. In the floor of the ulcer, formed usually by the submucous, sometimes by the muscular, and rarely by the peritoneal coat, small tubercles are developed, principally in connection with the blood-vessels and lymphatics, and as these are arranged transversely around the intestine, the new growth proceeds in the same direction. These nodules also soften and become caseous, and thus the process of ulceration gradually extends transversely until

a complete ring of the mucous membrane may be destroyed (*annular ulcer*). These appearances, together with the dilatation of the neighbouring vessels, may reveal the position of the ulcers before the bowel is opened. By the blending of adjacent ulcers most irregular figures are formed; and, in extensive cases, mere islets and bands of mucous membrane only are left in wide areas of the bowel. The ulcers thus produced (Fig. 141) present a strong contrast to those of typhoid fever. Bacilli are usually numerous and may be recognised in the stools by suitable staining.

The tubercular ulcer rarely, if ever, heals; but an ulcer *may* heal at one place, while it spreads at another, and the contraction of any scar-tissue that forms will lead to marked narrowing of the gut. Owing to the thickening of the tissues at its base, perforation is an



FIG. 141.—*A Tubercular Ulcer of the Intestine.* (Diagrammatic.
a. Epithelial lining. *b*. Submucous-tissue.
c. Muscular coat. *d*. Peritoneum.

exceptional occurrence. This takes place more commonly into a neighbouring viscus to which the ulcer has become adherent, than into the peritoneal cavity.

The lymphatic glands in connection with tubercular ulcers are generally affected. The lacteals leading from the ulcers, and even the thoracic duct itself, may be irregularly swollen by tubercles.

Tuberculosis of the Respiratory Tract.

The larynx and, to a less extent, the trachea both suffer from tubercle in its miliary and infiltrating forms.

Tubercle of the Larynx (**Laryngeal Phthisis**) may be primary, but is often secondary to disease of the lungs. It is said to commence as sub-epithelial tubercles situate chiefly in the ary-epiglottic folds, on the cords, and on the under surface of the epiglottis. These may be few or numerous, and may ulcerate early—especially on the cords—or may multiply and form a diffuse infiltration, which in the ary-epiglottic fold produces a pear-shaped swelling with its large end towards its fellow in the mid-line. Spreading ulceration ultimately occurs, perhaps leading to the formation of abscesses, to necrosis of

cartilage, and hence to hectic fever, exhaustion and death. Tubercular ulcers are distinguished from those due to syphilis, or to new-growths, by the small amount of new tissue in their floor and margins, and by the absence of cicatricial tissue.

Tracheal Ulcers are usually superficial. Occasionally they are very extensive.

Tuberculosis of the Lungs (Acute Miliary).—Tuberculous processes occur in the lungs as part of a general tuberculosis, and



FIG. 142.—*A small soft Grey Tubercle from the Lung in a Case of Acute Tuberculosis.* The whole of the tubercle is shown in the drawing, and is largely constituted of *intra-alveolar* products. × 100. Reduced to ⅓.

also in pulmonary phthisis. The nature of the resulting inflammatory lesions is similar in both. It will be well, however, in the present place, more particularly to describe these lesions as they occur in the general infective disease. The more limited processes which take place in phthisis will be again referred to in a subsequent chapter (see "Pulmonary Phthisis").

The pulmonary lesions met with in general tuberculosis consist, for the most part, of those disseminated nodular growths, which have been already described as **grey** and **yellow** tubercles (p. 384).

Both the *grey* and the *yellow* nodules are often found associated in the same lung; in other cases the grey nodules only are met with;

whilst, less frequently, nearly all the growths are of the yellow variety. The condition of the *pulmonary tissue* which is situated *between the nodules* varies considerably. It may be (1) perfectly normal; (2) more or less congested and œdematous; or (3) it may present varying sized tracts of greyish, granular, friable consolidation. A perfectly normal condition of the intervening pulmonary tissue is found in many of those cases in which all the growths are of the firm, grey variety; but when there are numerous yellow or soft grey nodules the lungs are nearly always more or less congested or consolidated. Although the virus is distributed by the circulation, the tubercles are usually present in greatest number at or near the apex—like the lesions in ordinary phthisis.

When these nodules are examined microscopically, they are seen to exhibit different kinds of structure. Some consist mainly of "giant-cell systems" as already described (p. 385), while others are characterised by accumulations of epithelial cells within the pulmonary alveoli. There is, however, this marked difference between the various kinds of nodules—that whereas the *small firm grey* ones are constituted almost entirely of the first-named structure, the *larger soft grey*, and most of the *yellow* ones, consist mainly of the intra-alveolar accumulations.

First, with regard to the *soft grey and yellow nodules*—most of these when examined with a low magnifying power present the appearance represented in Fig. 142, the nodules evidently consisting largely of accumulations within the alveolar cavities. When more highly magnified their constitution becomes more apparent. It is then seen that the alveolar cavities are filled with epithelial elements and small cells resembling leucocytes, whilst the alveolar walls are more or less extensively infiltrated and thickened with lymphoid cells (Fig. 143). In many cases the central portions of the nodules have undergone extensive degenerative changes and consist merely of a structureless granular débris, so that the accumulations

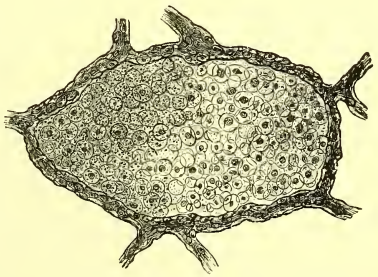


FIG. 143.—*A Portion of a small soft Grey Tubercle from the Lung.* This is from a case of acute tuberculosis, probably in an earlier stage than that from which Fig. 142 was drawn. The figure shows one of the alveoli filled with epithelial elements and a few small cells, with some cellular infiltration of the alveolar wall. × 200.

within the alveoli and the cellular infiltration of the alveolar walls are only visible at their periphery. This is always the case in the distinctly yellow tubercles (Fig. 144).

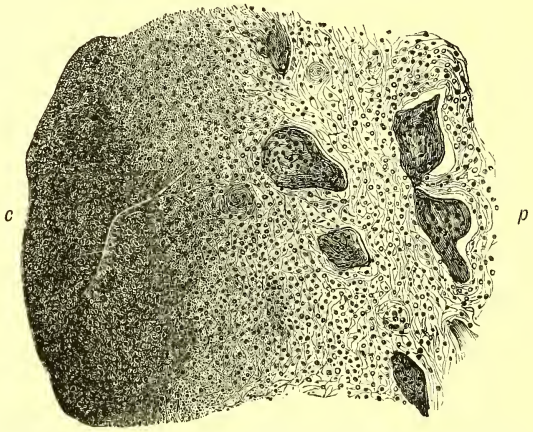


FIG. 144.—*A portion of a Yellow Tubercle from the Lung in a Case of Acute Tuberculosis.* Showing the degeneration of the central portions of the nodule *c*, and the cellular thickening of the alveolar walls and accumulations within the alveolar cavities at the periphery *p*. × 100.

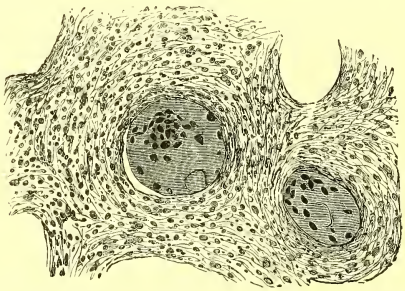


FIG. 145.—*A portion of the more External Part of a Grey Tubercle from the Lung in a Case of Acute Tuberculosis.* Showing the extensive infiltration and thickening of the alveolar walls, and the giant-cells within the alveolar cavities. × 100.

The histological characters of the *firmer grey nodules* differ somewhat from the preceding. In these, the cellular infiltration and consequent thickening of the alveolar wall are much more marked, and many of the

alveolar cavities are occupied by giant-cells. The origin of these is still uncertain. According to some, they are formed from the *alveolar epithelium* either by fusion of contiguous cells or by partial necrosis of the cell arresting its attempted proliferation (p. 388). Others regard them as due to a degenerative change of a similar nature in the *epithelioid* cells. According to Metchnikoff, they are due to the fusion of *mononuclear leucocytes*. In other cases, the alveolar structure has completely disappeared, and the tubercle, when examined with a low magnifying power, appears as a little spheroidal mass, the cellular

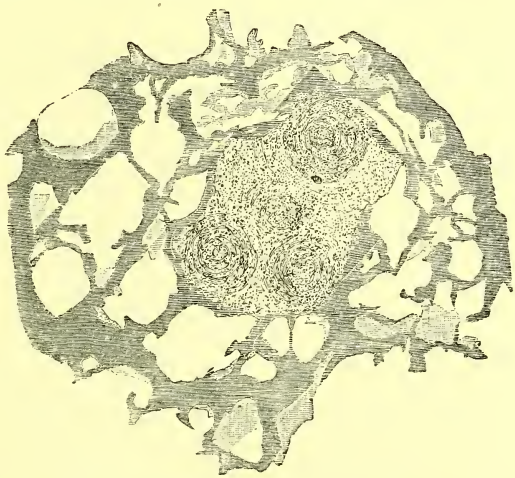


FIG. 146.—*A firm Grey Tubercle from the Lung in a Case of Acute Tuberculosis.* Showing the grouping of the elements around separate centres, the nodule consisting of several giant-cell systems. × 33.

elements of which are grouped around separate centres (Fig. 146). When more highly magnified, these centres are seen to correspond with the giant-cells already described, and with the small-celled structure grouped around them, as is well shown in Fig. 145. This is a fully developed tubercle of the lung. The small-celled structure at the peripheral portions of the nodules is replaced by a thickening of the walls of the alveoli with which the nodule is incorporated (Fig. 147). In the tubercles thus constituted, extensive retrogressive changes rarely occur. Degeneration is slow and very incomplete, and the nodule often becomes imperfectly fibroid.

Respecting the cause of these differences in the histological characters of the miliary lesions in the lungs—it may be stated that

while they depend to some extent upon differences in the age of the nodules, they are mainly due to rapidity of growth of the organisms. If these be numerous and multiply rapidly, the nodules will consist in the main of accumulations of epithelium within the pulmonary alveoli, and will rapidly undergo disintegration (see Fig. 143). If the growth of the bacilli be less active, typical "giant-cell systems" will form and the nodules will attain a more advanced age; while degeneration will be less rapid and complete (see Fig. 145). Lastly, if the organisms be few and their multiplication slow, as in the least intense and most

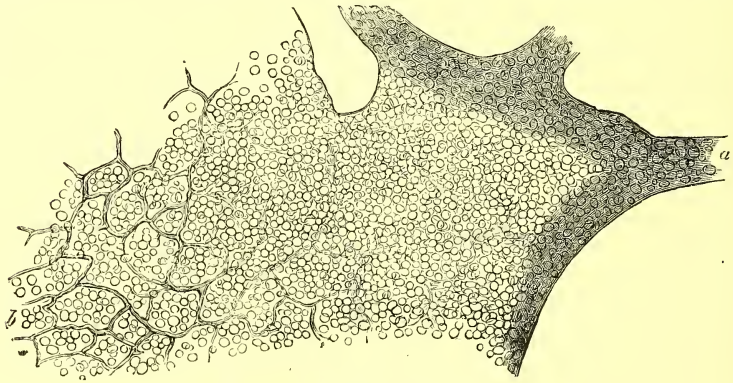


FIG. 147.—*A small portion of the most External Part of a firm Grey Tubercle from the Lung in a Case of Acute Tuberculosis.* Showing the incorporation of the nodule with the alveolar wall *a*. × 270.

chronic processes, the development of multinucleated elements and the proliferation of the tissue-cells reach their maximum (see Figs. 135 and 146). Degeneration takes place very slowly and is limited to the central portions of the nodule. There is often considerable fibroid induration of the new tissue. A close analogy can thus be drawn between the tissue-changes resulting from tuberculosis of the lungs and those which result from other chronic inflammatory processes (p. 276).

Tubercular Disease of Bones and Joints.

These may be conveniently taken together, as tubercular disease of a joint is frequently secondary to similar disease of a bone, and *vice versa*. The primary disease is, of course, due to infection through the blood; the secondary to extension from the primary focus.

In cases of acute general tuberculosis, both bones and joints may be the seats of *miliary tubercles.* In *bones,* the tubercles are found chiefly in cancellous parts; in *joints,* in the synovial and subsynovial tissues. They present no peculiarities and cause no local symptoms. It is said that miliary tubercles may be scattered through a bone without any general tuberculosis being present; and certainly multiple foci are not uncommon in the synovial membrane of a single joint.

Tubercular Periostitis and Osteomyelitis.—Periostitis and osteomyelitis when due to "tubercle" often coexist, just as they do when caused by other irritants. *Periostitis* cannot exist without a superficial *ostitis;* but the converse is not true, for a deep bony focus of tubercular inflammation may be present without any obvious involvement of the periosteum.

Seats.—Among the bones which are affected primarily are the bodies of the vertebræ, the ends of the long bones, the bones of the carpus and tarsus, the phalanges, and less often the metacarpal and metatarsal bones and the ribs. The shafts of the typical long bones are rarely affected by tubercular processes. The same may be said of the cranial bones; but certain bones of the face not uncommonly suffer.

The tubercular process more often starts in the bone than in the periosteum. Periosteal changes occasionally predominate in the case of the ribs, phalanges, and bodies of the vertebræ: when this is the case, early abscess almost always leads to their recognition. But in the vertebræ and probably in the phalanges, primary central changes are much the commoner.

Morbid Changes.—The order of events is much as follows. Bacilli are deposited at a certain spot, say in an epiphysis. Miliary tubercles next develop: a group of these becomes surrounded by a mass of granulation-tissue; and this again, in cases which are not progressing rapidly, and where irritation is not intense, by a zone of fibrous tissue. In this outer zone it is common to find the bony trabeculæ becoming thicker at the expense of the spaces—*i.e.,* the bone becoming sclerosed; more centrally, in the area of greater irritation, the trabeculæ are undergoing absorption.

From the primary focus, infection of the surrounding tissue occurs by means of fresh tubercles which form in the granulation-tissue zone. As these increase in number they gradually blend with the parent mass, which meanwhile has probably undergone caseation. But this widening of the area of infection leads to a corresponding widening of

the area of irritation ; the granulation-zone extends into and replaces the zone of fibrous tissue and of bony sclerosis, which in its turn reappears further from the centre. Thus the process spreads—now quickly, now slowly. Cure may be effected by the encapsulation of the caseous masses in fibrous tissue. This is sometimes followed by their calcification. On the other hand, the disease may spread till a surface is reached and the soft parts have become infected. Caseation of the tissue is synonymous with death, and any portion of bone separated *en bloc* by surrounding caseation forms a sequestrum. Usually only small fragments of trabeculæ are thus separated ; but sometimes caseation follows infiltration so rapidly that masses of bone as large as a filbert, or even larger, are detached. A whole epiphysis, such as the head of the femur, may thus die. As Cheyne has stated, the trabeculæ of the sequestra are often thickened, showing that a chronic inflammation preceded the change which caused the necrosis. This effectually disposes of König's hypothesis that the sequestra (which for some reason are often wedge-shaped) are due to embolism. Sometimes the sequestra consist of rarefied bone, and are soft and crumbling; sometimes the contents of the spaces are calcified. An abscess often forms with or without necrosis.

When the periosteum is primarily affected, the bone soon appears enlarged, owing to the growth of tubercles embedded in inflammatory tissue in the deeper layers of the periosteum and in the superficial Haversian canals. This growth may extend over a wide area of bone, or may penetrate deeply at one or more spots, eroding the bone as it grows, even after causing a preliminary sclerosis. Commonly an abscess forms, and either bursts or is opened. The rough surface of the infiltrated bone is then exposed. The cause of this softening of the tubercular tissue into a cold abscess is unknown ; but it seems certain that it is not due to infection with pyogenic organisms. Fluid and leucocytes find their way into the cheesy mass, which is broken up. We thus get a space filled with a milk-like fluid, often containing obvious cheesy masses and bits of bone. The wall of such an abscess is formed of dense fibrous tissue lined by a layer of granulation-tissue which can be easily detached.

On section, this wall shows, from without inwards, œdematous fibroid tissue, probably containing tubercles with central giant-cells; then granulation-tissue with numerous but less typical tubercles ; and, lastly, a layer, chiefly of epithelioid cells, which becomes more and more caseous as the cavity is approached.

Hyaline cartilage, being a non-vascular tissue, is never attacked primarily. Destruction of cartilage is sometimes due to the *spread inwards* over the surface of the cartilage of tubercular processes from the synovial membrane: these processes adhere like ivy, and gradually erode the cartilage, producing a cribriform appearance (Fig. 148). Similar destruction may also be due to the *perforation* of the cartilage by a mass of tubercular tissue sprouting through it from a focus in the subjacent bone; or to the *spread beneath* the cartilage of similar

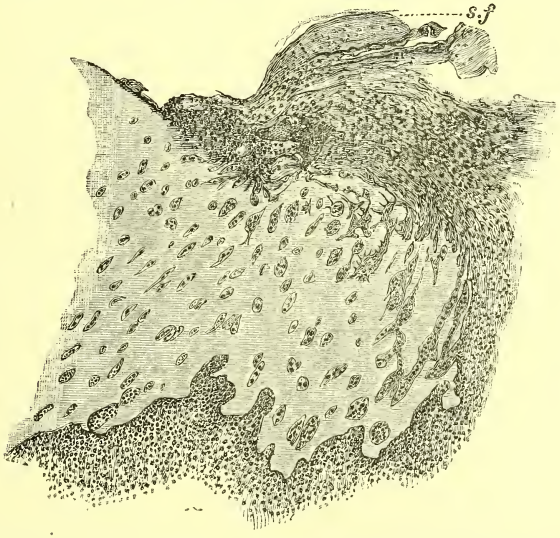


FIG. 148.—*Edge of Cartilage of Knee in Tubercular Arthritis,* resting upon inflamed bone, and markedly eroded on this aspect. The free surface of the cartilage is overgrown by a soft synovial fold (*s.f.*). Several channels, by means of which cells have reached the capsules of cartilage-cells, have been laid open. × 55. (F. T. Paul.)

tissue from a bony source. Large pieces of cartilage may be thus loosened from the bone, while still retaining a normal appearance on the side towards the joint. It is in one or other of the above ways that tubercular caries of the surfaces of the joint is established.

Tubercular Synovitis.

The tuberculous changes met with in the synovial membrane are the following: (1) *acute miliary tuberculosis,* as mentioned above; (2) *diffuse*

thickening (tumor albus)—by far the most frequent and important condition; (3) *nodular thickening* (synovitis tuberosa); (4) *hydrops;* and (5) *empyema.*

Diffuse thickening may be primary or secondary. When *primary,* it is due to the settlement of bacilli at one or more spots in the synovial or sub-synovial tissue. Tubercular masses grow and spread while the tissues round about become more or less swollen and gelatinous-looking from œdema and cell-infiltration. Clear or puriform fluid may be effused into the joint. The tubercular foci may soften and open either into the joint or into the periarticular tissues, or may form an abscess in the thickened synovial membrane. When *secondary,* the diffuse thickening may be due to bursting of a focus from the bone into the joint, and infection of the whole synovial membrane from within. After a little time this membrane presents the structure of the wall of a chronic abscess, and its cavity probably contains turbid or puriform fluid. At other times the thickening may be due chiefly to œdema of the synovial membrane excited by the presence of a focus in the bone, which has reached the surface at the reflection of the synovial membrane, and which has thus been shut off from the cavity of the joint. But at this point the membrane has been infected, and the tubercular tissue invading it excites much irritation and swelling in its neighbourhood. Cheyne states that in such cases he has been unable to discover any evidence of infection in the œdematous synovial membrane at a distance from the focus—a point of much practical importance.

In **synovitis tuberosa**, fungous masses of tubercular structure, from the size of a chestnut downwards, hang in greater or fewer numbers from the synovial membrane into the joint, which almost always contains fluid: this is often blood-stained. The membrane may be thick and deeply blood-stained towards the joint. Infection is through the blood primarily. Secondary infection from the membrane is unusual.

Tubercular hydrops is not distinguishable from the simple form, until thickening of the synovial membrane begins. König states that in early stages a thin layer of tubercular tissue can be found on the surface towards the joint.

Tubercular empyema is indistinguishable from tubercular hydrops until the fluid is drawn off: it occurs in old people and in highly tubercular subjects.

Lupus Vulgaris.

This disease is characterised by the appearance of reddish-brown nodules of granulation-tissue upon the *skin* (chiefly of the face), and much more rarely upon the *mucous membranes* of the conjunctiva, pharynx, vulva and vagina. The nodules are situate primarily in the corium, and at first are smaller than a pin's head, though they may reach the size of a pea; these blend to form a more or less diffuse mass, while fresh foci appear at the periphery. The disease generally *appears* between the age of two years and puberty, and is especially common in the obviously scrofulous: *recurrences* may occur again and again, and the disease may thus last, off and on, throughout a lifetime.

Structure.—The nodules consist of granulation-tissue containing epithelioid cells and often a good many giant-cells. They differ from true tubercles in being *rather richly vascular*. The intercellular substance is scanty and homogeneous. It is not uncommon to find that long anastomosing processes of epithelium have grown down into the round-celled growth, the physiological resistance (p. 123) of which would seem to be less than that of normal corium.

Course.—Spread occurs by the production of fresh nodules at the margin of the primary focus. The course is always chronic. When the patch has reached a certain size it may remain quiescent; the nodules and infiltration may end in degeneration and **absorption**, —a white scar being left—or in **ulceration**. After eating away the tissues to varying depths, sometimes destroying large portions of the nose, lip, or eyelid, the ulcers may heal; or healing may go on at one point and destruction at another. There is little or no tendency to caseation, and glands rarely become affected.

Ætiology.—The tubercle-like structure of the nodules has long been held to favour the surmise that lupus was a tuberculosis of the skin. This explanation of its pathology is now very generally accepted, though the proof is incomplete. In favour of its tubercular origin, it may be urged: (1) that a few tubercle bacilli are, in the large majority of cases, found in the affected tissues; (2) that pure cultures of tubercle bacilli have been obtained from such tissues; (3) that the inoculation of these cultures, or of the lupus tissue itself, will give rise to tuberculosis; (4) that injection of tuberculin is followed by an inflammatory reaction in lupus tissues; (5) that the structure of the tissue is such as would result from the very gradual growth of the

tubercle bacillus; and (6) that the temperature of the skin of the face is only a little above the lowest limit at which the bacillus will grow.

We may add that the bacilli have been found in tubercles excised before ulceration has begun. Some scrofulous lesion is often present in cases of lupus, and it is asserted that patients suffering from lupus—perhaps even the majority of them—die of some tubercular disease —*e.g.*, phthisis or meningitis.

The truth of the above is admitted by Kaposi, who, nevertheless, dissents from the view that lupus is a tuberculosis of the skin. His principal arguments against it are :—that even the frequent coincidence of scrofula and lupus proves nothing; that the bacilli are very few in number, and that *perhaps* the mode of staining is not really distinctive of the tubercle bacillus; that *tuberculosis* results from inoculation with lupus tissue—but *lupus* never; that there is no evidence of the contagiousness of lupus; and, lastly, that lupus remains lupus throughout its course, and never passes into scrofulo-derma and true tuberculosis of the skin. This statement is contradicted by many observers, and the balance of evidence certainly seems to favour the tubercular theory of the nature of the disease.

Scrofula.

The constitutional condition known as Scrofula is characterised * by a liability of certain tissues to become the seat of chronic inflammations, the causes of such inflammations being very slight and sometimes wholly hypothetical. It is generally believed that these tissues either possess congenitally, or acquire as a result of abnormal conditions of life, an *enfeebled resisting power against injury*. According to this view, slight or undiscoverable injuries, which have no effect upon a healthy subject, produce inflammation in the scrofulous. In this way the *abnormal susceptibility to inflammation* is explained.

The explanation given of the *abnormal chronicity* of the processes is very similar. Chronic inflammation always implies the prolonged or frequent action of a cause. It is almost impossible to keep an inflamed part out of reach of every possible cause of inflammation, such as friction, pressure, tension, and contact with foreign bodies. These

* A special type of countenance and body has long been held to characterise the scrofulous diathesis, but its scientific value is doubtful.

may be insufficient *to keep up* an inflammation in a healthy person, but in the vulnerable tissues of the scrofulous they are supposed to be sufficient for this purpose; and doubtless they do aid in rendering the process chronic.

This *susceptibility,* although more or less general, is commonly most marked in the mucous membranes and in the lymphatic glands. It is



FIG. 149.—*Scrofulous Inflammation of a Bronchus.* Section of a small bronchus of a markedly scrofulous child, the subject of bronchitis, which terminated in miliary tuberculosis. The deeper structures of the bronchial wall are seen to be extensively infiltrated with cells, most of which are *larger* than those met with in the less extensive infiltration of healthy inflammation. The infiltration extends to and invades the walls of the adjacent alveoli, which are seen at the upper part of the drawing. The cavity of the bronchus contains a little mucus, *m.* × 200. Reduced ½.

especially frequent in those glands which stand in direct relationship to the scalp, fauces, tonsils, and pharynx (cervical); with the lungs (bronchial); and with the intestine (mesenteric). These are the glands, it may be remarked, to which organisms are most likely to be carried. The skin (eczema impetiginodes), bones and joints (caries and chronic arthritis) are also very liable to be affected. The part which suffers varies in different cases, and *slight* injury (p. 324) is often the determining cause.

With regard to the tissue-changes occurring in scrofulous inflammation—it must be remembered that when inflammation occurs in a healthy individual, and does not cause the death of the part, the inflammatory products either become absorbed, or the process leads to suppuration, or to the formation of a vascularised connective-tissue. In scrofulous inflammation, on the other hand, the *absorption* of the inflammatory products is much less readily effected: they tend to *accumulate* in the tissues, where by their pressure they interfere with the circulation, and thus lead to retrogressive and *caseous* changes. Blood-vessels do not develop, and hence there is no organisation of the new growth.

The tissues of a part affected by scrofulous inflammation are usually infiltrated with cells. Here and there are opaque yellow caseous patches. Distinct tubercles are often recognisable by the naked eye. Giant-cells are especially frequent (Figs. 141 and 149). The infiltrated part contains but few vessels; hence the pale purplish look of the granulation-tissue which lines a chronic ("scrofulous") abscess and the pallor about a scrofulous joint (p. 418), as contrasted with the vivid red, vascular layer round a focus of acute suppuration. The anatomy of a scrofulous inflammation corresponds to that met with in the milder forms of tubercular irritation, in which proliferation of the tissue-cells forms the most marked change. Further, the course of a scrofulous inflammation—chronic, with *little* tendency to resolution, organisation, or suppuration, but with *marked* tendency to progressive degeneration, caseation, and softening—is precisely that which we see in tuberculosis of the lungs.

Moreover, scrofulous inflammations not uncommonly end in *acute miliary tuberculosis.* This is readily explained by the observation that tubercle bacilli are commonly present in small numbers, in the chronic inflammations of scrofulous type. From these, pure cultivations have been obtained, and successful inoculations have been made both with the cultivations thus procured and with portions of the diseased tissues (p. 393). The proof would therefore seem complete that *some scrofulous lesions are tubercular.* In all probability the *scrofulous diathesis* is identical with the *tuberculous diathesis.* It is well known that consumptive parents have scrofulous children, and *vice versa.*

Thus the *abnormal susceptibility* of scrofulous tissues, to which reference has been made (p. 420), appears in many cases to be reducible to this—that certain tissues or organs in the scrofulous are excessively predisposed to serve as hosts to the bacillus tuberculosis. That this

abnormal susceptibility does not always show itself seems certain for many reasons. After serious operations for strumous disease, speedy union can be readily obtained; after prolonged tearing and cutting operations upon diseased synovial membranes the results are excellent, provided that something like completeness is attained in removing the morbid and morbidly inclined tissue; and after scooping out the contents of scrofulous glands, the inflammatory process quickly subsides. No more rest or freedom from irritation is obtained for the wounded tissues after such operations than is given in other cases; often, indeed, less is obtained, and sepsis may be added—and yet, if the removal of the affected tissue has been complete, the parts do not again become the seats of the same intractable inflammation. And this is the case even when large portions of such "vulnerable" parts as epiphyses are left.

Against the view that scrofulous lesions are really tubercular, and that the scrofulous and tubercular diatheses are identical, has been urged the extreme frequency with which the mucous membranes and lymphatic glands in scrofulous children become the seats of obstinate and protracted inflammations which ultimately *end in recovery*. But recovery is possible even from phthisis (p. 393). It is no essential part of a tubercular process that it should end fatally, as experiments on animals and observations upon man fully show. Some of the catarrhs to which allusion has been made are due to the irritation of the tubercle bacillus; but the pathology of most of them is unknown. To admit that, in scrofulous children, the alimentary tract is especially liable to, and irritated by, abnormal fermentations, and that the bronchi are peculiarly prone to catarrh, is only to admit for the *scrofulous* what we have already allowed for the tubercular. Moreover, there can be little doubt that chronic bronchial catarrh facilitates tubercular infection. This would be a case of grafting a tubercular affection upon a simple chronic inflammation. To assume, however, that *all* scrofulous glands, bones, and joints have begun as simple inflammations, and that, if they recover, they have continued simple, but have become tubercular if they take an opposite course, is a conclusion unsupported by evidence and not in accordance with the fact that the products of many long-quiescent scrofulous inflammations will excite general tuberculosis if inoculated upon animals.

LEPROSY.

This disease is endemic in many parts of the world, especially in the East and West Indies, China, South America, and Equatorial and Southern Africa. From the fourth to the fourteenth century it was widely spread over Europe, reaching its highest point at the time of the Crusades, when thousands in England, France, Germany, and all round the Mediterranean suffered from the disease, and numerous leper-asylums for the isolation of the afflicted were founded. It began to die away at the beginning of the fifteenth century, and was relatively extinct by the end of that century, when syphilis first became prominent. Leprosy still lingers in many spots in Europe, particularly in Norway, Sweden, and Iceland.

VARIETIES.—There are two chief varieties of this disease—**tubercular** and **anæsthetic**. In the former the lesions affect chiefly the skin, in the latter chiefly the nerves.

In **tubercular** leprosy, patches of hyperæmia are followed by thickening of the skin and the formation of nodules, which may reach the size of walnuts. These changes are especially developed on parts exposed to the air—face, hands and feet—and appear sometimes singly, sometimes in groups. They may begin as distinct eruptions, separated by long intervals of time. The affected skin is first firm, and red or brownish; it then becomes soft and pale; unless injured, it does not, as a rule, ulcerate until long afterwards. When ulcers do form, they cause great destruction of features and other parts (*lepra mutilans*). Healing *may* occur. The nodules may affect other parts of the body, especially the extensor aspects of the limbs, and the mucous membranes of the eye, nose, mouth, and larynx.

In **anæsthetic** leprosy, cylindrical or fusiform swellings occur upon nerves, especially the ulnar and external popliteal. These swellings surround long portions of the nerves, affecting primarily the cutaneous and later the muscular branches. At first the skin is often painful and hyperæsthetic; later on it becomes anæsthetic, pale, and together with the paralysed muscles, wastes. A bullous eruption (*pemphigus leprosus*) in the area of the affected nerve may be the first sign of the disease: these bullæ may either dry, leaving pale insensitive patches, or they may be followed at once by ulcers. Sooner or later ulcers form upon the anæsthetic parts, leading to extensive destruction, and even to dropping off of fingers, toes, or large portions of limbs (*lepra mutilans*).

The two forms may run their course separately, but often occur together. The anæsthetic variety occurs chiefly in hot climates. In each form the glands receiving lymph from the diseased parts enlarge —first the superficial ones, then the deeper. Viscera—especially the liver, spleen and testes—may be also enlarged. In the tubercular form, death results from exhaustion or some intercurrent disease, after a course of eight or ten years: in the anæsthetic form, the duration is about twice as long.

HISTOLOGY.—To the naked eye, the new tissue, wherever situate, has the greyish or yellowish, semi-transparent, uniform

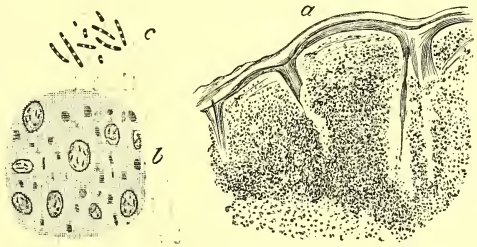


FIG. 150.—*Tubercular Leprosy.* Section through skin. *a.* Showing infiltration with leprosy bacilli. × 6. *b.* Showing bacilli in the cells. × 300. *c.* Individual bacilli showing spores (?). × 800. (Thin.)

appearance common to so many structures. The loose areolar tissues are chiefly affected; and in a less degree, lymphoid tissue. Microscopically, the nodules consist of four principal elements. (1) Large numbers of small and often vacuolated epithelioid cells, generally containing bacilli (*vide infra*), and frequently found in the lymph spaces, from the endothelial cells of which they are possibly derived. (2) Large masses, known as "lepra cells," containing one large vacuole and often a number of smaller ones, as well as bacilli, granules, and occasionally many nuclei. These lepra cells may be found inside lymphatics, or encircling lymphatics or atrophied sweat glands; according to Metchnikoff, these are large mononucleated leucocytes which have "engulfed" the bacilli. (3) Clumps of free bacilli in the lymphatics or elsewhere. (4) An overgrowth of fibrous tissue.

The new tissue in the skin ultimately undergoes degeneration and is absorbed, or breaks down. The foci run together, and the diseased part appears on section to be divided into nodular masses by fibrous

bands. Other tissues may, on account of the interference with their nutrition, necrose or atrophy.

The lymphatic glands contain small fibrous patches. As Delépine points out, the liver, spleen and nerves all show signs of chronic interstitial inflammation. The lungs are often said to be tubercular. They certainly have the appearances of organs undergoing caseous bronchopneumonia; but that this condition is really due to a *separate cause*, such as tubercle, is doubtful.

ÆTIOLOGY.—From time immemorial, leprosy has been looked upon as a contagious disease, and lepers have been rigorously excluded from social communities. A very superficial examination throws doubt upon this; for in many cases lepers have been known to live in the closest association with healthy people without communicating the disease. Many observers have maintained that the disease is communicable under certain conditions which are rarely realised. It seems more difficult to prove the contagiousness of leprosy than that of phthisis, and it certainly is not so great.

It may be noted that leprosy flourishes in all climates and upon all soils; that poor diet, and salt fish, do not appear to be special factors in its ætiology, as some have thought; and that the disease does not seem to be hereditary, although Hirsch held firmly to the opposite conclusion. Children born of leprous parents in leprous places may acquire the disease, but so may outsiders entering such a place. Possibly there may be some slight hereditary predisposition analogous to that believed to exist in the case of phthisis.

Observers are agreed that there is constantly present in all the recent primary lesions of leprosy a bacillus very closely resembling in its characters the tubercle bacillus (p. 395). So close is this resemblance that the chief point of interest in the pathology of this disease at the present moment is to determine whether the two organisms are *separate* species, or only modifications of *a single* species.

The bacilli found in leprosy may vary in shape, size, and staining affinities. Delépine showed that in a single patient, the bacilli free in the tissues were shorter and more readily stained than those in the lepra cells; while those in the skin and mucous membranes were longer and more rapidly stained than those in the liver and spleen. The bacilli are difficult to find, both in the neighbourhood of ulcerating surfaces and in the lungs. They are said to occur in definite clumps (Hansen), and to be thus distinguishable from tubercle bacilli.

Attempts to cultivate the organism have so generally failed that the few recorded exceptions are of little value until more fully confirmed. Amid conditions under which the tubercle bacillus will flourish, the leprosy bacillus will not even grow at all.

Nor do inoculation-experiments give decisive results. In the case of a criminal, the disease followed inoculation—offered as an alternative to execution—but the man had up to this point been in frequent contact with lepers. Whether the affected tissues be introduced into other parts of leprous patients, or into animals, the results are uniformly unsuccessful, though the bacilli themselves are not destroyed, for they can be found months afterwards in the tissues.

The constancy of the association between (1) a certain set of clinical manifestations, (2) a fairly definite series of pathological changes, and (3) the invariable presence of a special bacillus, constitutes the greater part of the evidence in favour of the view that this organism is a distinct species and the specific cause of the disease. It at present remains uncertain whether the organism is a modified form of the tubercle bacillus or not. Delépine thus sums up the evidence in favour of the view that it is such a modification:—"(1) The characters of the bacillus and its staining reactions. (2) The nature of some of the lesions. (3) The frequency of phthisis and scrofula in leprous patients (over twenty-five per cent.) or in their antecedents. (4) The difficulty of obtaining any result from inoculation with the most typical and advanced leprotic lesions. (5) The success of inoculation with products obtained from organs less typically affected, such as the lungs. (6) In cases of successful inoculation, the production of a disease which is generally tuberculous, or indistinguishable from tuberculosis." *

It seems strange, if this view be correct, that the reversion to the original type does not take place more frequently, and that leprosy as a clinical entity does not disappear.

SYPHILIS.

The lesions occurring in the course of constitutional syphilis also belong to the class of Infective Granulomata. They are inflammatory

* The student is referred to a very able description of a case of this disease by Delépine in *Trans. Path. Soc. of London*, vol. xlii. p. 386, 1891.

in their nature, but in their seats, distribution, sequence, and histological characters, present certain peculiarities which make them characteristic of this disease. The primary syphilitic lesion (usually the *indurated chancre*) occurring at the point of inoculation, is followed by enlargement of the neighbouring lymphatic glands; and, later on, when the virus becomes generalised, by a series of changes in the skin and mucous membranes. At a still later period these may be succeeded by changes in the nervous system, bones, and internal organs, most of them the results of inflammatory processes induced by the syphilitic poison. Though not yet certainly recognised, the nodular nature of the lesions demonstrates the particulate nature of the cause, and the multiple foci of disease prove its power of multiplication. Syphilis has now taken its place in the classification of disease as a "chronic general infective disease."

APPEARANCES.—I. **Early Lesions.**—Many of these are anatomically indistinguishable from simple inflammations of the same parts. The rashes, for example, are due to inflammatory hyperæmia with more or less infiltration of the superficial layer of the skin, enlargement of the papillæ, and, often, excessive epithelial multiplication. As a rule these inflammations end naturally in resolution; but in tissues of feeble resisting power they may ulcerate. Early syphilitic periostitis (*nodes*) is indistinguishable from traumatic inflammation, and syphilitic iritis is diagnosed from rheumatic only by concomitant circumstances.

II. **Later Lesions.** — The most frequent, but not the most characteristic, of these changes, is **fibroid induration**. Anatomically, this is ordinary productive inflammation, ending in scar-tissue (p. 276). When the fibrous tissue is gradually developed without evidence of any change, except such degeneration and atrophy as may depend on the subsequent contraction of this tissue, it is sometimes spoken of as an overgrowth of connective-tissue. Its appearance, however, varies in different cases and in different parts of the same organ. Sometimes the new tissue consists almost wholly of cells with but little intercellular substance, sometimes of cells in a markedly fibroid matrix; and, at others, of dense fibrous tissue only. The infiltration *may* be general, but much more commonly the fibroid areas are separated by comparatively healthy portions of the organ. It is the *irregular distribution* of these lesions which makes them so *characteristic of syphilis.*

The capsules of organs are *irregularly* thickened any peritoneal

coverings they may possess are sure to be involved ; and more or less general adhesion to surrounding parts occurs. These changes are seen in syphilitic hepatitis, splenitis, and orchitis. In the orchitis, the coincidence of hydrocele proves during life the affection of the tunica vaginalis. The irregular thickening of the capsule is the most marked feature.

As the fibrous tissue contracts, the organ shrinks and often becomes of stony hardness ; but the irregular distribution of the exudation often causes unequal contraction and puckering of the surface, amounting in some cases to the formation of deep fissures which almost divide the organ into lobes. In these cases the diffuse growth has probably been combined with the gummatous, and the thickened capsule is connected with fibrous rays which extend deeply into the surrounding tissue.

Naked-eye examination of a testis, which has undergone these changes, shows adhesions between the layers of the tunica vaginalis, with intervening spaces containing fluid, marked thickening of the tunica albuginea and, extending from it into the organ towards the mediastinum, dense bands of fibrous tissue. The natural reddish-brown colour of the tubules is replaced by a much paler whitish-yellow tint, in which islands of normal tissue may remain. The consistence of the gland is greatly increased. One or two gummata may also be present.

When occurring in bone, formations of this kind often ossify. Under the periosteum, they cause thickening of the bone. In the Haversian canals and cancellous spaces they lead to increase in its density.

These cell-formations do not always go on to fibroid induration ; they may resolve, and, under the influence of iodide of potassium, generally do so with marvellous rapidity, provided they are at all recent. Probably the inflammatory products undergo fatty degeneration previous to absorption.

Gummata, Syphilitic Tumours, Syphilomata.—Anatomically these are the most characteristic lesions of syphilis ; they are frequently associated with the fibroid induration just described. As usually met with, they are moderately firm yellowish-white nodules, having on section an appearance suggestive of the cut surface of a horse-chestnut. They vary in size from a hemp-seed to a walnut, and are surrounded by a zone of translucent fibrous-looking tissue, which sometimes has the appearance of a capsule, and which is so intimately associated with the surrounding structures that enucleation of the mass is impossible.

The outline of the growth is generally irregular owing to the number of fibrous processes which radiate from it along the natural septa of the organ. In the *earlier* stages of their development, when they less commonly come under observation, gummata are much softer in consistence, more vascular, and of a reddish-white colour ; whilst in their most *advanced* stages, owing to extensive degenerative changes, they may be opaque, yellow, and fatty.

Examined *microscopically*, gummata are found to vary in their minute structure according to their age. When **recent** they are divisible into three zones. The *central* portions are composed of closely

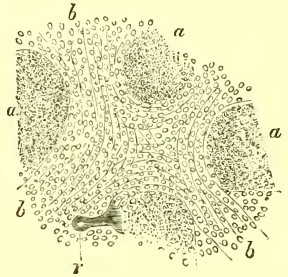


FIG. 151.—*Gummy Growth from Liver. a.* Central portions of growth consisting of granular débris. *b.* Peripheral granulation-tissue. *r.* A blood-vessel. × 100. (Cornil and Ranvier.)

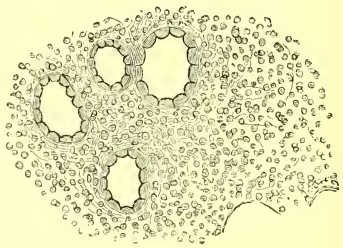


FIG. 152.—*The Peripheral Portion of a Gummy Growth in the Kidney.* Showing the small-cell granulation-growth in the intertubular-tissue. × 200.

packed shrunken cells and nuclei, fat granules and cholesterin, amongst which is generally a little fibrillated tissue (Fig. 151, *a*). Surrounding this and directly continuous with it is the *intermediate* zone, consisting of epithelioid cells in a distinctly fibrillated matrix. The *peripheral* portion of the growth (Fig. 151, *b*, and Fig. 152), which is in direct histological continuity with the surrounding structures, consists mainly of leucocytes, though epithelioid and even giant-cells are also found. Giant-cells are much rarer than in tubercle. The cells are separated by a scanty, homogeneous, intercellular material and numerous new blood-vessels.

In **older** gummata, only two zones may be apparent, an *inner* or *caseous* zone and an *outer* or *fibrous* zone. The origin of the cells in each case is most likely the same as in tubercle. It seems probable, however, that the chemical effects of the syphilitic virus are less deadly

to the life of the new cells than are the corresponding effects of the tubercular. The further development of the new tissue therefore proceeds, and vessels are formed. The caseation which next occurs is not so much due to the direct action of the virus as to the subsequent shutting off of the blood-supply. By means of changes, presently to be described, the walls of the blood-vessels in the centre of a gumma become thickened, and in thickening, encroach upon and nearly obliterate the lumen. Subsequent thrombosis in the affected vessels completes the interference with the blood-stream. To these changes must also be added the strangulating effect on the blood-vessels, produced by the contraction of the new fibrous tissue. The parts thus gradually deprived of blood must degenerate, and this occurs at a comparatively early stage, although not so early as in tubercle. When the gumma is large, and particularly when the epithelioid cells are present in large numbers, the mass may be seen to be made up of an agglomeration of smaller growths, each having the characteristic structure. When the leucocytes especially predominate, the foci run together and their outlines are lost.

In *early* stages, before they have produced marked destruction of tissue, gummata may disappear. In *later* stages their *central* fatty portions are frequently absorbed, leaving a radiating puckered scar: calcification is rare. Not uncommonly, under conditions which are not understood, gummata soften and excite suppuration around them; the abscess bursts, and a yellow slough is exposed. This has a very characteristic appearance, like "wet wash-leather"—tough and coherent, very unlike the dead tissue thrown out from the caseous centre of a tubercular focus. It gradually becomes detached, leaving a larger or smaller cavity with soft ragged margins. These changes can often be seen in the tongue. Gummata of the *skin* and *mucous membranes* are the most prone to take this course. These ulcerations must be distinguished from the superficial ulcerations connected with the early rashes.

Gummata are met with in the skin and subcutaneous cellular tissue; in the submucous tissue, especially of the pharynx, soft palate, tongue, and larynx; in muscle, fasciæ, and bone; and in the connective-tissue of organs—especially of the liver, brain, testicle, and kidney. Gummata also occur, but much less frequently, in the lungs, especially in *congenital* syphilis: simple localised fibroid indurations are found under the same circumstances. They generally form late, or "tertiary," manifestations; but they *may* occur at quite an early

stage. No hard line can be drawn *clinically* between the secondary and tertiary stages, and none can be drawn *pathologically* between the products of these stages. Most are inflammatory: of these some are circumscribed and some diffuse. Even the hard chancre has the same structure as the first stage of a gumma—leucocytes, epithelioid-cells, and giant-cells in a fibrillar matrix.

At various places, attention has been drawn to resemblances and distinctions between tubercular and syphilitic formations. The points

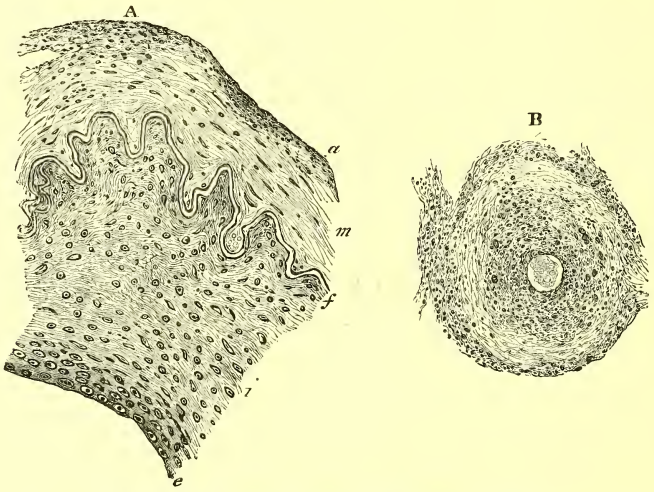


FIG. 153.—*Syphilitic Disease of Cerebral Arteries.*

A. Segment of middle cerebral artery, transverse section—*i*, thickened inner coat; *e*, endothelium; *f*, membrana fenestrata; *m*, muscular coat; *a*, adventitia. × 200. Reduced ½.

B. Small artery of pia mater, transverse section. Showing thickened inner coat, diminished lumen of vessel, and considerable infiltration of adventitia. The cavity of the vessel is occupied by a clot. × 100. Reduced ½. (Barlow.)

of contrast may be thus summarised. In syphilis (1) the contagion is more easily traceable; (2) the foci are larger, and show a greater tendency to organisation, while endarteritis of their vessels is invariable; and (3) the lesions are always local, and pigmentation is common.

Changes in Vessels.—Certain changes in the arteries, known as *Endarteritis obliterans*, occur in syphilis.

In the cerebral arteries the changes produce opacity and marked

thickening of the vessel, with considerable diminution in its calibre. It is this diminution of the lumen of the vessel which is especially characteristic. The smaller vessels, arteries and veins, are chiefly affected, and their lumina may be quite obliterated.

When tranverse sections of the vessels are examined microscopically, the principal change is seen to be situated in the *inner* coat (Fig. 153). This coat is considerably thickened by a cellular growth. The growth, which is limited internally by the endothelium of the vessel, and externally by the membrana fenestrata, seems to consist of "productive" inflammatory tissue (p. 276).

In addition to this change in the intima, the outer coat is abnormally vascular and infiltrated with small cells (Fig. 153), and this cellular infiltration usually invades the muscular layer as well. The marked diminution of the lumen of the vessel, and the consequent interference with the circulation, coupled with the changes in the endothelium, frequently lead to coagulation of the blood (*thrombosis*) and cerebral softening (pp. 60, and 250).

ÆTIOLOGY.—Strong as is the *clinical* evidence of the infective nature of syphilis, nothing positive is known of its cause. The general similarity between the lesions of syphilis and those of the other infective granulomata, lends weight to the supposition that the virus is an organism which enters through a mucous membrane or through an abraded surface of skin, and is carried into the blood indirectly by the lymphatics, and directly by the blood itself; for the early destruction of an infected surface fails to prevent the general disease.

The poison exists in the primary sore, in mucous tubercles, and all secondary sores, and in the blood during the eruptive period. It is doubtful whether it is present in pure lymph, such as may be obtained from a vaccine-vesicle. It is not present in normal secretions, as saliva, mucus, semen. The discharge from tertiary or gummatous ulcers is not infective.

Klebs inoculated apes with portions of syphilitic tissue, and produced a disease closely resembling syphilis.

During recent years, many observers have described organisms which they have found in syphilitic lesions. None of these results have up to the present time been sufficiently confirmed. Lustgarten, in particular, has described a bacillus very similar if not identical with that usually present in the smegma preputii. But in this, as in other cases, nothing certain is yet known.

Syphilitic Disease of the Liver.

The liver is one of the most frequent seats of syphilitic lesions. The most common change is the development of fibroid and gummy growths in the substance of the organ. In the spreading stage, the margins of gummata are ill-defined, round cells infiltrating the surrounding liver-tissue. The growths—which are usually connected with fibroid thickenings of the capsule and adjacent peritoneum—sometimes consist simply of a dense fibroid structure. More commonly, however, gummata are found embedded in this fibroid growth. In the former case, it is possible that the gummata may have become absorbed. In congenital syphilis, *recent* gummata are frequently met with.

The development of these growths produces very marked alterations in the form of the liver. Scar-like depressions are seen on its surface, and the organ is irregularly and often very deeply puckered.

A more general fibroid change, not associated with the formation of gummata, is occasionally met with in the liver in congenital syphilis. This change closely resembles ordinary cirrhosis, although the intercellular network of the liver is usually more extensively involved.

Lastly, it must be mentioned that the liver in syphilis is frequently lardaceous.

It is unnecessary to describe the syphilitic lesions which occur in other organs, as they all present the same general characters—viz., cell-infiltrations, scars, fibroid indurations, and gummata, singly or combined.

Certain chronic degenerative changes in the nervous system are attributed to syphilis among other causes. The degeneration of the nerve-tissue is accompanied by an apparent overgrowth of neuroglia. The syphilis probably acts by interfering with the nutrition of the cell-dendrites, and atrophy of the fibre follows (see Chapter xxxii.).

GLANDERS AND FARCY.

These are varieties of one disease, due probably to difference in the point of entry of the poison. In **Glanders**, the nasal mucous membrane and its prolongations are the seat of the earliest lesions; in **Farcy**, the skin and subcutaneous tissue. Each form may run a rapid or a slow course, and in man it is usual for the symptoms of the

one to supervene sooner or later upon those of the other. The diseases are common among equine animals, especially horses, and are communicable from them to other animals, including man. This happens but rarely. The disease is also transferable from man to man.

NATURE OF THE LESION.—The characteristic lesions in farcy correspond to some intermediate stage between an acute abscess on the one hand, and a typical tubercle on the other. They are best seen in the more **chronic** varieties. A circumscribed nodule (**farcy-bud**) appears, varying in size from a just visible point to that of a pea or bean. On section this is found to consist of small round, and epithelioid cells: vascularisation is at best very imperfect. Degeneration occurs early, and more or less acute suppuration follows. When a farcy-bud forms near a free surface, an ulcer with a sharply cut indurated margin and a very foul base usually results. Such ulcers may heal, but their course is generally very chronic. In the more **acute** forms of the disease, the poison sets up ordinary suppuration at the spots where it develops. The inflammation is not always circumscribed: sometimes it is diffuse, giving rise to infiltration of muscles, subcutaneous tissue, and the connective-tissue of the orbit. This is succeeded by suppuration at several points, or throughout the infiltrated tissue.

COURSE OF THE DISEASE.—A wound is a common place of entry; mucous membranes, especially the conjunctival and nasal, are also seats of primary infection. In many cases there is no evidence to show how the poison has entered.

In **acute glanders**, after a variable period of incubation, inflammatory nodules appear in the mucous membrane of the nose, frontal sinuses, or other places, and run on more or less rapidly to suppuration and ulceration. The submaxillary and cervical glands swell—from infection through the lymphatics. The fever and muco-purulent or bloody discharge from the nostrils are thus explained. The poison now enters the blood and is carried to distant parts, giving rise to metastatic inflammations in the lungs and other internal organs, in the skin, and in the mucous membranes of the respiratory and alimentary tracts. Abscesses in the subcutaneous and intermuscular tissues are common, and suppuration in joints occurs. In fact, the disease resembles pyæmia in many respects, being, like it, due to the dissemination by the blood of a poison capable of exciting suppuration.

The abscesses in organs are generally small, but may reach a large size. The respiratory and alimentary mucous membranes are perhaps directly infected from the nose. On the skin, red papules and larger patches of inflammation appear. On these, vesicles and then pustules —often with hæmorrhagic contents—quickly develop. These constitute the rash of the disease. The earliest stage is a collection of round cells in the superficial part of a papilla; a little later a pustule is found

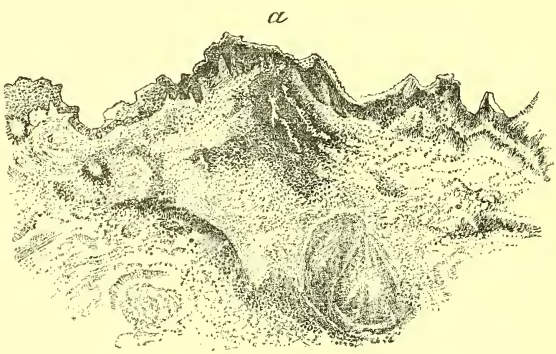


FIG. 154.—*Section through a "Bud" in the Skin from a Case of Acute Farcy.* The horny layer has mostly disappeared and the Malpighian layer is pushed upwards by the subjacent abscess (just below *a*). The mass of pus-corpuscles is just breaking down to form a cavity, the walls of which are infiltrated with similar cells. (From a specimen by Mr. Boyd.)

to have developed under the rete. The fever is high throughout the disease, symptoms of prostration appear early, and death occurs with all the signs of septic poisoning.

In **Chronic Farcy** large "buds" appear in the subcutaneous, submucous, and intermuscular tissues. The "buds" near the surface break down slowly, and form foul ulcers, the lymphatics become much swollen, hard, and knotted; the glands are greatly enlarged. The general symptoms are much milder. This form often ends in recovery. The symptoms of acute glanders frequently supervene before death.

ÆTIOLOGY.—In the pus of abscesses in glanders, Schülz and Lœffler found slender rods, smaller than, but resembling generally, the bacilli of tubercle. Cultivated in the serum of horse's blood, these rods formed colonies, maintaining their initial form. After repeated cultivation, to ensure purity from the original pus, different animals

were inoculated. The result varied with their susceptibility. In all, an indurated ulcer appeared at the site of inoculation; and cordy lymphatics ran thence to swollen glands. In some, metastatic abscesses formed in internal organs; in others, death occurred rapidly, with symptoms of septic poisoning. In all, the above bacilli were found. Two horses were inoculated from a fourth cultivation: after some days' incubation, the symptoms of glanders set in, and the older horse died in fourteen days. The other was extremely weak and was killed next day. The post-mortem signs were the same in both—viz., a sore the size of a shilling at the site of inoculation; hard and swollen lymphatics, leading thence to glands; abscesses in the lungs, from the size of a pea downwards; farcy buds and ulcers studding the nasal mucosa.

By this one series of experiments, it would seem that this bacillus has been proved to be the cause of glanders and farcy.

An extract of the cultures has been prepared and is known as *mallein*. When injected subcutaneously in cases of glanders, it gives rise to an inflammatory reaction at the seat of the disease. In doubtful cases animals are therefore injected with mallein as an aid to diagnosis (p. 345).

RHINOSCLEROMA.

This disease was first described in 1870. It is equally distributed between the sexes, and occurs in people of all ranks of life between the ages of fifteen and forty. The only case recorded in England, occurred in the person of a Guatemalan under the care of Semon and Payne. There has been no reason for suspecting any connection with tubercle, syphilis or other widespreading disease: anti-syphilitic treatment has always been without effect.

APPEARANCES.—The disease consists in the formation of flat or elevated, sharply defined plaques or masses of new growth which are hard, tender, and elastic. Their primary seat is in the skin or mucous membrane near the anterior nares, which they obstruct. They first force the alæ nasi apart and render them so rigid that little impression can be made upon them: indeed the nose below the bones has been compared to ivory or plaster-of-Paris. From the front of the nose they may spread to the upper lip and even round the whole mouth—greatly narrowing the orifice—and thence to the gums. More commonly

however, they spread from the nasal orifices back through the nasal cavities (both sides being soon affected), block the lachrymal ducts, and reach both hard and soft palate, which become infiltrated, while the latter is also disfigured by scar-contraction. The infiltration may spread to the pharynx and glottis, inducing rigidity and closure of the latter orifice, and consequent aphonia and dyspnœa. In a case reported by Kaposi, one of the cheeks was involved to such an extent, that the nose seemed, by comparison, depressed. Similar changes have been described in both external auditory canals, and in the external auditory meatus. The growth has never been known to generalise, and for years the health remains unaffected. When the disease is not interfered with, extension is slow, but continuous. Recurrence has invariably and rapidly followed even apparently complete removal.

The masses round the nostril are like keloid or hypertrophic scars. They are light or dark brownish-red in colour, and here and there smooth and fissured. The skin around is quite normal. There is little or no tendency to ulceration—after years it may just be excoriated. Injuries excite little or no reaction: after removal of a piece, it recurs and skins over.

HISTOLOGY.—Dense infiltration of the corium with small round cells is found. The cells lie in a stroma which is frequently fibrillated, and usually presents some dense bands, upon which Payne supposes the great hardness of the growth to depend; in some cases, however, cartilage and bone have been found in the stroma. Many of the cells are spindle-shaped, and a few may be epithelioid, but large cell-forms are the exception. The growth is tolerably vascular and presents no tendency to fatty degeneration. Cornil describes some of the cells as containing "hyaline masses," which may also be present in the tissue.

As in lupus, down-growth of epithelial processes into the granulation-tissue of the corium is usual.

ÆTIOLOGY.—The question of contagion has not been raised; but the disease is regarded by most authorities as an infective granuloma on account of its morbid anatomy, coupled with the constant presence of a bacillus (Frisch), said by different observers to occur in the cells, lymphatics or tissues. Payne figures them in all three situations.* The bacilli are short and thick, ovoid, or even round, and two are often

* *Trans. Path. Society of London*, 1885.

bound together as diplococci in a capsule. The organism has been cultivated: it grows rapidly at 97° to 100° F. Inoculations made with the culture or with pieces of the growth upon the noses of dogs, have always failed. Proof of the ætiological relationship between this germ and the disease is therefore defective. It has been suggested that the organism is possibly a modified form of Friedländer's pneumo-bacillus. According to Mibelli, the "hyaline masses" consist of the "shed" capsules of the organisms.

ACTINOMYCOSIS.

This disease consists in the formation of small sarcoma-like tumours or abscesses, containing a peculiar ray-like fungus—the actinomyces. This fungus is supposed to be the exciting cause. The commonest seats are the lung and liver, but the fungus may be found in any part. It is more commonly met with in animals than in man. In cattle the disease most often affects the jaws.

In 1878 Israel described a case of multiple superficial abscesses, with one large intrathoracic abscess opening by fistulæ on the surface. The pus, from all, contained parasites which corresponded to the above description. The disease had begun six months before with fever and joint-pains. Three weeks after admission the woman died. A large abscess was found in the left lung, and countless abscesses existed in the liver, spleen, intestine and kidneys: most of them were very small, but some were as large as an apple. All contained the fungi, and in the glomeruli of the kidney were found organisms which had not yet excited inflammation.

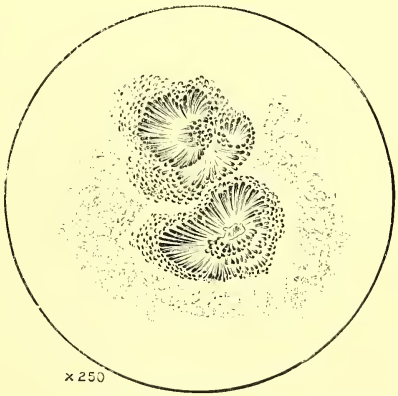


FIG. 155.—*Actinomyces*. From the tongue of the ox. Two masses of club-shaped radiating filaments are seen.

APPEARANCES. — On section these nodules have a spongy open appearance, and a puriform or cheesy fluid can be squeezed

from them. Besides fatty cells, this contains many pale yellow granules, as large as millet-seeds. These, when gently squeezed and cleared up by potash, are seen to consist of filaments radiating from a common centre, and bearing at their free ends club-shaped swellings, often branched, and frequently calcified (Fig. 155). Threads and spherical bodies are found less frequently. The nodules and abscesses also contain granulation-tissue, intersected here and there by bands of fibrous tissue. In the older specimens there are found, round each fungus, the usual signs of a chronic inflammation caused by a slight, constant irritant (p. 276).

Israel states that the fungus may enter in three ways—

1. **From the Mouth**—through a carious tooth or extraction-wound. By one of these channels it reaches the interior of the jaw and grows there. It next bursts through the outer plate, and gives rise to an abscess in the glands or connective-tissue of the neck. It is probable that infection may take place through the follicles of the tonsil in tonsillitis or of the pharynx in pharyngitis (*prevertebral abscess*).

2. **From the Respiratory Passages.**—In one case, only chronic bronchitis seemed to be present, but the sputum contained the actinomyces. Usually the fungus sets up a caseous broncho-pneumonia, similar to that met with in phthisis, but shut off from the healthy lung by a layer of healthy granulations which are succeeded by dense fibrous tissue. The cavities run together, the symptoms being very like those of phthisis, though marked hæmoptysis is uncommon. Then, adhesions having formed over the diseased area, the fungus spreads to the posterior mediastinum, through the diaphragm into the peritoneum (causing *peritonitis*), liver or spleen (*abscess*), or into the anterior mediastinum and pericardium. Lastly, some of these abscesses after much burrowing find their way to the surface. It is noteworthy that, though the actinomyces affects the lungs from above down, like the tubercle bacillus, it leaves the apex—above the clavicle—uninvolved.

3. **From the Intestine.**—The intestine may be affected primarily from within, or, secondarily, by embolism or by extension from other organs. The primary form may lead merely to catarrh—or to the development of foci in the submucous tissue or mucosa, which break down into ulcers with undermined edges reaching down to the muscularis. Perforation into the peritoneum, into other hollow viscera or through the abdominal wall may result.

In a good many cases the channel of infection remains doubtful.

Actinomycotic embolism may lead to abscesses accompanied by symptoms of pyæmia: secondary growths may occur anywhere. Ponfick has seen a granulation-mass growing into the jugular vein, in a case in which there were growths in the right auricle and ventricle.

For some time all attempts to cultivate the organism failed. This failure has been attributed to the fact that only the *club* forms were used, and that these are incapable of cultivation. If the *threads* be taken, amber-like beads appear on the culture-ground. The colonies thus obtained consist of *threads* and *spheres*, but *no clubs*. Inoculation of the cultures gives rise to the characteristic lesions, including the presence of both the *club* and *thread* forms of the parasite. The exact botanical position of the fungus has not yet been determined.

SOURCES OF INFECTION.—Israel thinks that in some of his cases he has been able to eliminate the possibility of infection through diseased beef or pork, and that the germ must have entered with water or vegetables. Water is *unlikely* as a nidus, for it soon destroys the adult fungus; but Jensen has traced an epidemic of actinomycosis in Iceland to eating rye grown on soil recently reclaimed from the sea.*

CHAPTER XXIII.

SEPTICÆMIA AND PYÆMIA.

The diseases known as Septicæmia and Pyæmia result from the absorption and dissemination of substances usually derived from the septic discharge of some wound or acute inflammation. The two diseases are frequently associated.

By "Septicæmia" is now generally understood those forms of septic disease which are unaccompanied by the development of secondary inflammations. "Pyæmia," on the other hand, is a term used to denote those cases of septic disease which are characterised by the presence of secondary or metastatic abscesses. These two maladies are the chief elements in the excessive mortality in large surgical hospitals, and nothing is more clearly established than that overcrowding of

* Israel: *New Sydenham Society*, vol. cxv. Delépine: *Trans. Path. Society of London*, 1889.

patients with septic wounds is, indirectly, their chief cause. By this process the disease may speedily be generated anywhere. In almost every case of each disease, there exists a wound which has been infected by some germ-bearing air, finger, instrument or dressing, or which may have been inoculated directly from a similar case.

SEPTICÆMIA.

EXPERIMENTAL RESEARCHES.—Koch *injected* five minims of blood, or meat-infusion, in an early stage of putrefaction, under the skin of house-mice. In each case the animal at once grew restless and ceased eating, its movements became weak and uncertain, its respiration irregular and slow, and death occurred in four to eight hours, or even earlier—the time of its occurrence varying with the amount of putrefactive material injected. No pathological change was found in the body, and no effect was produced by inoculating healthy animals with the blood. Thus the disease was *not infective*. It was clearly due to the absorption into the blood of putrid material, unaccompanied by any secondary inflammation: it was therefore a *septicæmia*. Furthermore, it seems to have been due to the presence of a chemical poison in the blood, for the result is comparable to the injection of a poisonous alkaloid. Such a substance would exercise its specific action upon the organism, and would *not multiply* in the body; so that the effect would naturally vary with the amount injected; while, even in a rapidly fatal case, a few drops of the blood would contain so small a fraction of the original dose, that, if injected into a healthy animal, they would have no effect. This form of septicæmia is called **Septic Intoxication** or **Sapræmia**. From an extensive series of experiments Burdon Sanderson gives the following as its symptoms:—restlessness and muscular twitching, followed by weakness increasing till the animal falls; vomiting and profuse diarrhœa, the fæces being at first loose and whitish-grey, but later bloody; a temperature at first raised some degrees, but often sub-normal before death; gradually failing respiration and cardiac action; and death sometimes preceded by cramps. The corresponding post-mortem appearances are:—blood dark and feebly clotted; petechiæ beneath pericardium, endocardium, and pleura; intense staining of the endocardium and lining membranes of the great vessels, and often a little blood-tinged serum in the serous cavities, both occurring so soon after death, as to indicate destruction of the red corpuscles even during life; intense congestion

and ecchymosis of the mucous membrane of the stomach and intestines with shedding of the epithelium; spleen swollen, soft, and pulpy; liver often swollen and congested.

When less poison was introduced, the resulting symptoms were less marked, and when only one or two drops of putrid blood were *inoculated*, no change was immediately apparent. Indeed, after the introduction of such small quantities of blood, the mice often remained permanently well. But after an interval of some twenty-four hours, about a third of them sickened, the symptoms being characteristic and constant, and not preceded by the above toxic effects. The eyes became dull, the conjunctival secretion increased until the lids seemed glued together; the animal moved little and languidly, and generally sat still in some peculiar attitude; it ceased to eat, its respirations became slower, its weakness steadily increased, and death came on almost imperceptibly forty to sixty hours after inoculation. Post-mortem there were found:—slight œdema, which is often absent, at the site of the injection or inoculation, and considerable swelling of the spleen: other organs appeared normal.

To cause death with these symptoms in about fifty hours, it is only necessary to touch with a knife the subcutaneous tissue of a mouse, dead of the disease, at any point however remote from the seat of inoculation; and then, with this knife, to scratch the ear of a healthy animal.

Here, again, we have a disease which must, according to our definition, be called *Septicæmia*. But it differs from that form first described, in being intensely *infective*. Only a minute quantity of poison is introduced—quite insufficient to produce toxic effects—but it *multiplies* enormously in the blood. Some twenty-four hours of incubation pass without symptoms, until its development reaches a certain stage. Then symptoms appear, and with the further increase of the virus, the symptoms also increase proportionately. This form is known as **Septic Infection.**

The blood of animals which died after the *injection* of 1 to 10 ℥ of *putrid blood*, generally contained varying numbers of cocci, bacteria and bacilli; but the blood of those that died after the *inoculation* last described contained only small bacilli. These were present in large numbers, most white corpuscles containing one or more of them. Koch thinks they grow into the vessels about the seat of inoculation, and thus become generalised; he has never seen them in lymphatics.

They occur in all parts, and are not more numerous in the swollen spleen than elsewhere.

Under the heading Septicæmia, we have therefore two diseases: (1) **septic intoxication**, or **Sapræmia**, a non-infective disease, due to the absorption of a chemical poison manufactured in some putrefactive process external to the body, and often ending fatally before any organisms introduced have time to develop to an extent sufficient to produce symptoms; and (2) **septic infection**, due to the entry of specific fungi into the blood and to their multiplication there. The organisms act by producing poisonous substances in their growth, but these products are not "irritants," and therefore no secondary inflammations arise. The fungi which characterise the septicæmia of one animal differ from those which occur in that of another—*e.g.*, bacilli in mice, oval cocci in rabbits. Every putrid fluid does not necessarily contain the organisms of each of these diseases. The production of septic infection from putrid fluids is therefore uncertain. Many different organisms are probably capable of producing septicæmia.

OBSERVATIONS ON MAN.—In Man the occurrence of analogous forms is, *à priori*, likely, and cases might be quoted in which the existence of *septic intoxication* or *septic infection* was very probable; but the subject has not been at all fully worked out. Clinically, it is usually impossible to diagnose between them; and the post-mortem signs are very similar. The **symptoms** of septicæmia in Man often begin with a rigor, which may be repeated, especially in the infective form; this is accompanied by rise of temperature, and all the symptoms of fever, with delirium passing on to stupor or even coma. These are followed by great loss of strength and rapid emaciation; a dry tongue, and a rapid, feeble pulse complete the phenomena characteristic of the "typhoid state." Vomiting is frequent and much commoner than diarrhœa; but cases do occur in which the symptoms and pathological changes of gastro-enteritis are well marked. A jaundiced tint of skin is not uncommon, and petechial spots may occur. Albuminuria is frequent. In the *infective* form death occurs quietly in a semi-comatose state. In the *non-infective* form, the ending is more rapid. The patient becomes collapsed and dies with dyspnœa, and all the symptoms of rapid cardiac failure.

The red corpuscles, in blood withdrawn during life, run into clumps instead of rouleaux; and Hüter states, as the result of observations on

the palpebra tertia of infected animals and on the lip of man, that in septicæmia there is widespread capillary stasis. In severe cases, the blood in half the capillaries of a district may be stationary. Frequently, too, small clumps of red corpuscles pass across the field or stick in some vessel.

Post-mortem.—The rigor mortis is feeble, and decomposition sets in early. The blood may be dark and fluid, but is more often clotted in the usual manner; soon after death, there is deep staining of the endocardium and lining membrane of the great vessels, and any serous fluid in the pleural or pericardial cavities will be blood-tinged—this is owing to rapid disintegration of red corpuscles, which begins before life ceases. Petechiæ occur beneath the serous membranes, and are commonest on the back of the heart and under the pleuræ. Hypostatic congestion of the lungs, congestion of the abdominal viscera, swelling and pulpiness of the spleen, and congestion, or, much more rarely, inflammation of the mucous membrane of the alimentary canal complete the list of changes.

Organisms, especially cocci, have been found in various places in about half the cases of septicæmia. Even in these cases, no characteristic form has been shown to be present.

Marcus Beck calculated from the result of experiments on dogs, that 1 to 2 oz. of putrid serum or pus would be required to kill an adult man by **septic intoxication**. This form can, therefore, occur only where *large cavities* exist and *are imperfectly drained—e.g.*, in bad compound fractures, in wounds of joints or pleuræ, in abdominal sections, or in the uterus after labour. Sometimes such cavities cannot be efficiently drained: hence the necessity for preventing putrefaction of their contents. Raw surfaces and serous membranes are well known to be excellent absorbent surfaces. A large quantity of poison may be taken up by them in a short time. Granulating surfaces on the other hand, as demonstrated by Billroth, do not absorb the putrid poison. Hence **septic intoxication** will be most likely to occur *before granulation begins*. It may occur later if the granulation-tissue is destroyed in any way. No line can be drawn between it and septic traumatic fever (p. 260).

Septic Infection may occur from the smallest wound, and there may be distinct evidence that some poison has been inoculated. The presence of only a *small wound* is evidence of septic infection as opposed to septic intoxication.

With regard to the cause of septic intoxication—many of the

products of putrefaction are capable of producing fever. Bergmann succeeded in obtaining from putrid fluids an alkaloidal body which he called *sepsin*. This body crystallises in fine needles, and possesses in a high degree the property of exciting fever.

PYÆMIA.

Pyæmia differs from septicæmia in this respect, that in it the absorption and dissemination of the poison give rise not only to a general disease, but also cause the formation of secondary foci of inflammation — so-called **metastatic abscesses**. These are the distinctive pathological characteristics of the disease. Its clinical symptoms are well marked, the very irregular temperature being most important; but it is confessedly complicated with more or less septic poisoning.

Like septic infection, the disease is essentially a hospital-disease, and their poisons are probably similar; some indeed believe them to be the same. The source of infection is almost always some inflammation or suppurating wound, with septic discharge. But there may be no wound, as is seen in acute infective periostitis, infective endocarditis, and those rare cases of "spontaneous" pyæmia in which no primary lesion can be found. In these cases the poison has probably entered through some healthy mucous membrane. As in septicæmia, it gains access to, and is distributed by, the blood.

Besides the secondary abscesses, the following signs may be found **post-mortem**. As in all septic disease, rigor mortis is feeble and decomposition early. Emaciation is generally marked, and the skin yellow or jaundiced. Petechiæ may be present. The wound, if there be one, is sloughy, perhaps surrounded by diffuse inflammation, and offensive. Any bone which has been divided shows the appearances of septic osteomyelitis. The thrombi in the veins leading from the focus of infection are extensive, and are undergoing infective puriform softening (p. 233); the ends of one or more thrombi perhaps project into a large vein in which the circulation was not arrested. The blood is generally normal to the naked eye, but microscopically it contains an excess of leucocytes. Hypostatic congestion of the lungs is generally present, the spleen is large and pulpy, and the liver and kidneys show "granular degeneration."

The **secondary abscesses** are of *two kinds:* (1) those which follow upon infarction, and (2) those in which there is no evidence of such an

antecedent change. In either case, the occurrence of suppuration implies the presence of a strong irritant acting for some time, and it has already been pointed out (p. 292) that most irritants of this kind are fungi. It is probable that several fungi are capable of exciting suppuration, and any one of them might, if generalised by the blood-stream, produce the abscesses of pyæmia. It seems possible, therefore, that the organism which produces acute necrosis is not always the same as that which gives rise to ordinary pyæmia from wounds. The *streptococcus pyogenes* (p. 350) is the organism most often present.

However this may be, in the *first* kind of abscess, infarction is induced by the lodgment in a terminal artery of a portion of an infective clot. The mode of formation and characters of the infarct and abscess have been described on pp. 241 and 280. A probable source of embolism has been noted above in the account of the veins leading from the focus of infection. These embolic abscesses are most frequent in the *lungs*, but may be found in the liver, spleen, kidneys, and brain. They may occur in any vascular part. They lie generally upon the surface of organs, with their bases immediately beneath the capsule. They vary in size between that of a chestnut and that of a split pea, are usually multiple, and may be very numerous. They are surrounded by the usual hyperæmic ring. Often more than one organ is affected, and these abscesses may occur with others of the next kind. Sometimes the *lungs* escape while other organs, lying beyond them on the blood-path, are affected.

The *second* kind of abscess is a diffuse suppuration occurring in the subcutaneous and intermuscular connective-tissue, in the joints and in the serous membranes. In these cases the irritant must be conveyed to the spot by the blood and lodge there, either because the nidus is suitable, or because some capillary embolism has occurred. This form of suppuration may occur alone or be combined with the first variety.

Pyæmia has never been produced in animals by the injection of blood or pus from pyæmic patients. Cocci and zooglœa-masses are found in abundance on the surface of the focus of infection, the intensity of the process often varying with their number. They have been traced into the surrounding tissues, and have been seen piercing the wall of a vein. They have been found in the nearest lymph-glands, in all metastatic abscesses, and in many organs. They lie primarily in capillaries or small arteries, but soon pass out into the surrounding tissues.

Koch injected 10 ℳ of putrid fluid, in which a portion of skin had

been macerated, into a rabbit. No symptoms followed for two days; then the animal ate less, became weaker, and died 105 hours after the injection. A purulent infiltration of the abdominal wall around the point of injection, was found; the inflammation had extended to the peritoneum, and there was general fibrinous peritonitis. The spleen was much enlarged, the liver had a greyish mottled appearance, and grey wedge-shaped patches appeared on section. In the lungs were some dark-red airless patches about as large as a pea. Animals inoculated with the blood died of precisely the same disease. The smaller the dose, the longer the time before death. This is explicable only on the supposition that the infective particles in the blood must reach a certain number in proportion to the body-weight before they can cause death. Micrococci were found everywhere, especially in obviously altered parts. They adhered to the interior of vessels, often plugging them. Red corpuscles adhered to the coccus colonies, which seemed able to induce coagulation; small thrombi were thus formed, which could be swept away to form infective emboli. Perhaps something of this kind may account for the second kind of abscess, but against this is the fact that pyogenic cocci are sometimes found in human blood, causing no such aggregations and no abscesses (p. 324). In such cases, however, the cocci are introduced without any pabulum on which they can thrive. The resemblance of the whole disease to pyæmia is very marked. It is not certain, however, that pyæmia in man is *always* infective. In other words, secondary abscesses *may* be due to emboli derived from putrid clots containing only non-pathogenic organisms, incapable of growing among active tissues or in the blood.

CHAPTER XXIV.

MALARIA.

Malaria is the name which for many years has been employed to denote the virus of a frequently fatal disease, occurring principally in tropical climates, and characterised by periodic attacks of fever. When these attacks recur *daily*, the disease is known as *quotidian* ague, when on *alternate* days, as *tertian* ague; when every *third* day, as *quartan* ague. The periodicity is not always so regular or so simple,

nor the intervals so short, as in these examples. When the individual febrile recurrences run into each other so that there are no apyretic intervals, but only slight remissions, the term "remittent fever" is applied to the attack. Pathologically, the disease is associated with great enlargement of the spleen, and marked pigmentation of many parts—*e.g.*, spleen, liver, and brain. It is the type of an endemic disease: it is strictly limited to particular localities; that is to say, it can be acquired in these localities only, although its clinical manifestations may develop elsewhere. It is never communicated directly from person to person except by the direct intravenous inoculation of blood taken from an individual in whose blood the germ is present.

Laveran first pointed out that if a careful examination be made of a drop of blood, taken from a malarial patient during, shortly before, or, in certain types of the disease, some time after, one of these febrile attacks, certain characteristic appearances will be found. No staining is necessary or indeed advisable; but it is essential that very thin layers of blood be obtained, so that the corpuscles may be in a single layer, lying flat, and not forming rouleaux. An oil-immersion lens should be used. It may be necessary to spend an hour in the search before the organism is discovered; but usually it can be seen in every second or third field of the microscope: and sometimes even five or six parasites are present in each field. In this way the observer will be able to demonstrate the presence, especially in the red corpuscles, of one or more of the following bodies:—(1) circular or ring-shaped amœboid discs, pale and apparently structureless, lying on or in the red corpuscles, and not unlike vacuoles (Fig. 156, 2, 3); (2) pigmented amœboid bodies occupying from a sixth to almost the whole of the affected corpuscle, which usually contains only one such body (4, 5); (3) well defined rosette-shaped or clustered bodies, the segments surrounding or radiating from a clump of pigment, in or about the centre of the figure (6)—these may be free in the plasma or may be encircled by the remnant of a red corpuscle; (4) pigmented crescentic bodies (6 *a*); (5) flagellated organisms and free flagella (5 *d, e, f*; 6 *e, f*; (6) leucocytes containing black pigment; (7) all, any, or fragments of the above which have escaped or have been expressed from the corpuscles.

The appearances will be better understood by reference to the accompanying drawings. The horizontal series is arranged according to the views first formulated by Golgi, and now held by Manson and others, concerning their life-history in the blood; though it must be

remembered that as development does not progress when the bodies are removed from the circulation, the complete cycle cannot be actually observed. The two parallel vertical series represent observed changes,

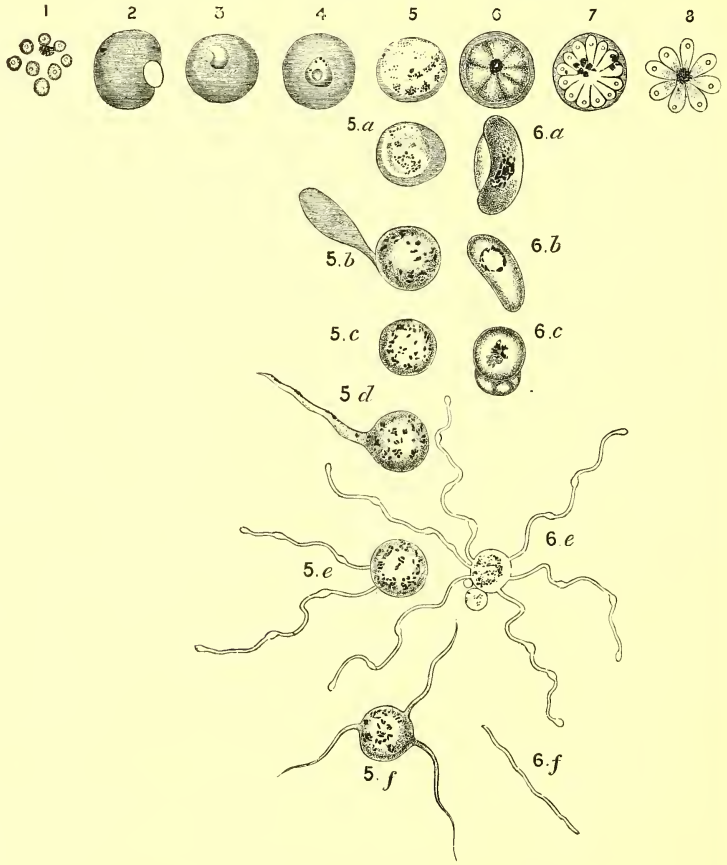


FIG. 156.—*Parasites from the Blood of Patients suffering from Malaria.* An explanation of the above figures, which have been taken from various sources, is embodied in the text.

believed to be possible developments of the pigmented amœboid bodies (5). As these only occur after the parasite has been removed from the circulation, they are considered by Manson to form a provision for carrying on the life of the malarial organism outside

the human body, and during its passage from one human being to another.

1 represents the most minute forms which are found free in the plasma; 2 and 3 are believed to show that these minute bodies become attached to, and penetrate, the corpuscles; 4 and 5 show the growth of the intra-corpuscular discs and the development and distribution of the pigment. During these stages, amœboid movements may be easily observed in the parasite, as well as distinct, extensive, and sometimes rapid motion among the pigment particles, manifestly not of the nature of "Brownian" movement. The pigment is believed to be an excrementitious product—the unused remains of the hæmoglobin digested by the parasite. The next figure (6) represents the organism as a perfectly circular disc, almost completely filling the corpuscle. The pigment is now aggregated in the centre, and faint indications of commencing segmentation are discernible. A little later this circular disc divides into distinct segments, and these form an almost perfect rosette (7). The remains of the corpuscle in the meantime fall away, while the segments separate and are thrown into the general circulation. They are then supposed to form the minute circular bodies first mentioned, and, if they escape the phagocytes, to seek inclusion in red corpuscles as before described.

In the first of the two vertical columns, are represented different stages that have been observed, showing that, under some circumstances, certain of the parasites have the power of leaving the corpuscle, and of developing into a flagellated organism. The flagella appear quite suddenly, as if they had developed beneath a capsule, which, giving way, allows them to spring out and obtain room to act. These flagella lash the surrounding fluid, and cause much commotion; they then become detached, swim about for a time, and slowly disappear. They exhibit two kinds of movement, the one slower and undulating, the other quicker and quivering—as of a stiffened rod.

In the parallel column, another sequence of changes from the same body (5) is shown. The crescentic bodies, according to Manson's view, seem to be a result of the circular, centrally pigmented discs becoming curved on the flat, their form depending on mechanical necessities accruing from continued enlargement of the parasite in an unyielding red corpuscle—hence the position of the pigment. The crescents first become straight and cylindrical, then oval, and finally spherical. The pigment then becomes diffused, all trace of the enclosing corpuscle disappears, and a flagellated organism is formed as in the previous case.

The crescents and their progeny are the most persistent of all, and resist the attack both of phagocytes and of quinine. Flagellated organisms are never found until the blood has been withdrawn for about a quarter of an hour. They are therefore supposed not to exist as such in the body at all, but to form stages in the life-history of the parasites outside the body. In what forms, and in what places, this existence is passed is unknown. Manson draws a parallel between the conditions and requirements of the malarial parasite in the circulating blood, and those of the filaria sanguinis hominis, and argues that as the parasite does not escape with any of the secretions, it can only be removed by some suctorial insect, such as the mosquito, just as in the case of the filaria.

There can be no reasonable doubt that the bodies described are phases in the life-history of a protozoal parasite; hence it is known as the "hæmatozoon malariæ," sometimes as the "plasmodium malariæ." Until the life-history outside the body has been traced, and malarial disease induced by the inoculation of it in this phase, the proof that it is the cause of malarial disease must be considered imperfect; although the presumption is strongly in its favour. Thus it is invariably found during the paroxysm; it is never found in persons not suffering from malaria; and blood containing it can alone transmit the disease.

The administration of quinine is followed by the disappearance of the intra-corpuscular parasites: the crescentic bodies are the last to go. Leucocytes have been seen to approach and touch the intra-corpuscular forms, though they never *enclose* any but the extra-corpuscular.

The commencement of the fever-paroxysm coincides with the breaking up of the rosette-body. In different forms of malarial fever, the duration of the life of each generation of parasites corresponds with the cycle of the fever; thus it is forty-eight hours in tertian, seventy-two hours in quartan, and in quotidian there is a double infection of two or more generations of parasites.

The severer types of malaria, found in warm countries, are generally associated with the formation of the crescentic bodies, while the early stage of the parasite assumes a ring-shape; in these, the rosette-body is rarely found in finger-blood, but may be present in that withdrawn from the capillaries of the spleen, brain, and other organs during life or after death.

The malaria of more temperate latitudes is never associated with the formation of crescents, the flagellated body being formed directly

from intra-corpuscular discs which escape from the red corpuscles. In the severer and more malignant types of malarial fever, many of the affected corpuscles appear to necrose, shrivel, and deepen in colour: these constitute the "brassy bodies" of the Italian writers. In such fevers small ring-shaped parasites, crescents, these "brassy bodies," and pigmented leucocytes, may be the only bodies found in finger-blood, the large quantity of pigment in the leucocytes indicating the extensive formation of rosette-bodies in the viscera.*

CHAPTER XXV.

INFLAMMATION OF THE CONNECTIVE-TISSUES.

The *process* of inflammation is much the same, wherever it may occur. Every tissue in the body may be inflamed; but whilst inflammation is common in some organs and tissues, it is rare in others. Certain forms of inflammation occur with especial frequency in certain parts, and the appearances will necessarily vary with the part involved.

The student should be perfectly familiar with the different forms of inflammation, so that their names may at once revive in his memory a picture of the special changes already described, as well as of their causes and consequences.

Inflammation of Connective-tissue.

Common connective-tissue accompanies blood-vessels everywhere. When vessels are injured, this tissue is more likely than any other to share in that injury; and if the vessels alone are damaged, it will be the first structure to experience the effects of the lesion. Thus, every form of inflammation occurs in connective-tissue; the whole description of the process applies to it.

With regard to special varieties of connective-tissue, the **non-vascular**—**cornea** and **cartilage**—are especially interesting as the battle-grounds upon which the origin of the new cells in inflammation have been fought. Senftleben's experiments (p. 266) have shown that injury of the cornea produces none of the vascular signs of inflamma-

* For further information the student is referred to vols. cxlvi. and cl. of the New Sydenham Society's works, and to articles by Manson in *The Lancet* and *Brit. Med. Journ.*, 1894.

tion unless the marginal vessels are affected, or unless leucocytes are admitted from the conjunctival sac. About the third day after destruction of cells, regenerative processes set in. Observations on cartilage are more difficult, but they show that the above results hold good.

Inflammation of the Cornea.

Anteriorly and posteriorly the cornea is limited by membranes sufficiently stout to resist the passage of leucocytes; but, in inflammation, leucocytes and fluid-exudation from the vessels enter freely from the margin, passing along the lymph-channels in which the cells and nerves lie. The leucocytes thus accumulate in clusters around the corneal cells. Such exudation is accompanied by softening and opacity of the corneal structure, and may lead to alteration in its curvature. This happens in vascular keratitis and the interstitial inflammation of congenital syphilis. When a slight vascular exudation forms beneath the roughened epithelium as a consequence of the irritation of granular lids, the condition is known as *pannus*. Pus, forming between the layers of the cornea, constitutes *onyx;* and ulcers in all stages are common. They heal by scar-tissue, and leave an opacity and a more or less altered corneal curve. Any keratitis may be "productive," and result in opacity and altered curve.

Inflammation of Cartilage.

In the most acute inflammations of joints, the cartilage may slough bodily, as the cornea does in the worst cases of conjunctivitis, from injury and lack of nourishment. It then either peels off in flakes, or softens and wears away at points of pressure. In less acute cases it may be invaded by leucocytes from the joint-cavity or from the bone (p. 417). Multiplication of cartilage-cells may be seen, even though leucocytes naturally tend to collect in their capsules (Fig. 157); but in rheumatoid arthritis—if, indeed, the disease is inflammatory—multiplication of the cartilage-cells is the characteristic lesion, and is continued until the distended capsules burst into the cavity of the joint. Regenerative changes probably occur in chronic cases. In a joint with inflamed cartilages, the fluid is always turbid from degenerating leucocytes and their products—thus differing from that of serous synovitis; and under certain conditions the transition to pus

is easy. Healing takes place by the formation of scar-tissue from the new cells. Short, extremely strong and wide adhesions often bind the surfaces together, producing *fibrous ankylosis*. If the bone is involved some or all of the adhesions will ossify—*bony ankylosis*.

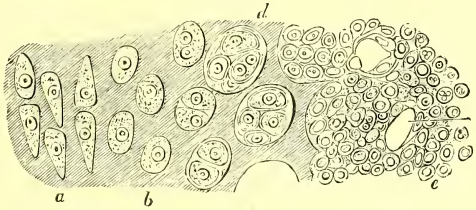


FIG. 157.—*Section of Inflamed Cartilage.* *a*. The normal cartilage cells. *b*. The same enlarged. *d*. Multiplication of cells within their capsules. *e*. Eroding layer of granulation-tissue. × 250. (Cornil and Ranvier.) Some of the cells are probably invading leucocytes.

Inflammation of Bone.

Inflammation of bone always originates in its vascular structures—the periosteum and medulla. **Periostitis** implies that the *periosteum* is inflamed, but the adjacent layers of the *bone* are always involved. When the inflammation chiefly affects the medulla and other soft parts lying in the Haversian canals or cancellous spaces, the condition is called **ostitis**; but when the medulla in the canal of a long bone is most markedly involved, the term **myelitis** is employed. Inflammation is never strictly limited to either of these parts; hence the term **osteomyelitis.**

PERIOSTITIS.—A **serous** form is described. It is rare, and is the mildest form of infective inflammation of the part. The exudation is highly albuminous.

Fibrinous and **productive** inflammations are common as the result of injury and syphilis. A projecting node is formed. This consists of proliferated cells from the deeper layer of the periosteum, as well as of emigrated leucocytes. These cells may disappear, or may, as in other cases, be succeeded by fibrous tissue. This may ossify: it very rarely breaks down. Ossification begins in that part of the new tissue which is in contact with the surface of the bone. The vessels entering the Haversian canals in the latter are, on account of the elevation of the periosteum, more or less vertical to

the surface ; hence the new Haversian canals have the same direction. These new canals are, at first, well defined and easily separable from the old, but both ultimately become indistinguishably blended. Later on, in syphilis, when gummata form beneath the periosteum, it is common for suppuration and superficial caries to occur. The subcutaneous bones are chiefly affected. Inflammatory thickening of a bone is always due to periostitis.

Suppurative periostitis is generally a part of the infective disease known as **acute necrosis** and **osteomyelitis**. This disease is generally associated with injury. It affects growing bones, and rarely, if ever, occurs after union of the epiphyses. It is generally believed that pyogenic organisms lodge in the medulla, excite suppuration, and then spread through the Haversian canals to the periosteum, and there set up the same process : possibly the organisms may affect the periosteum primarily and alone. Pus, forming beneath this membrane, rapidly separates it from the bone. The vessels passing inwards from the periosteum are thus greatly stretched, and this, together with the primary damage to the vessels, induces thrombosis in many of them. Hence *superficial* necrosis is the usual result ; and if the medulla also has suppurated, the necrosis will be *total—i.e.*, will involve the whole thickness of the shaft. Pyæmia often follows before the abscess is opened ; and this is the condition in which infective fat-embolism is most likely to occur. In **septic osteomyelitis**, following operations in which the medullary cavity has been opened, a diffuse suppurative inflammation attacks the medulla and periosteum, causes total necrosis of large portions of bone, and very frequently produces a fatal result from pyæmia (p. 446).

OSTITIS (osteitis).—The mildest form described is that in which granulation-tissue is produced. This occurs much oftener in cancellous (vertebræ, tarsus, carpus, epiphyses of long bones) than in compact bone. A round-celled infiltration takes place in the medulla and presses into the Haversian canals ; the fat-cells and the hard substance of the bone disappear before it—cancellous trabeculæ are eaten through and Haversian canals widened. A section shows spaces crowded with cells, often developing here and there into fibrous tissue. On the surface of the bone, bordering these spaces, are seen semilunar erosions, as if small bites had been taken out of it. These are called Howship's lacunæ. Each contains leucocytes and epithelioid cells, and often a giant-cell. The giant-cells erode the

bone. The normal bone-corpuscles remain unchanged so long as they are distinguishable. This process is called **rarefying ostitis**, and is an ulceration or **caries** of bone without formation of pus (*caries sicca*). Nothing is more natural than that a bone thus weakened should yield to pressure; thus the bodies of vertebræ may almost disappear, those above and below becoming approximated; while the shafts of long bones bend, as is seen in *ostitis deformans* and other diffuse inflammations. The inflammatory tissue may pursue any of the courses mentioned on pp. 276 *et seq.*

In a very early case, absorption of the inflammatory exudation may occur, and regeneration make good any loss. But when marked destruction of bone has occurred, scar-tissue must form and ossify, if a cure is to be effected. This is what happens in cases of spinal curvature without abscess. Too often, however, the cells degenerate and soften, more or less "suppuration" occurs, and a **cold abscess** results (p. 279). When this is opened, the ulcerating, **carious**, surface of bone is exposed. If healing occur, it is by the development of healthy granulation-tissue, followed by scar-tissue, which subsequently ossifies. Tubercles are almost always found in such carious processes. Syphilis is another cause.

Death and breaking down of the infiltrating granulation-tissue leads to death of the infiltrated bone: the pieces which come away are generally of small size—**caries necrotica.**

In the most chronic forms of ostitis no rarefaction of bone occurs; the new growth slowly ossifies, and the Haversian canals and cancellous spaces diminish. The bone consequently becomes extremely heavy and ivory-like; it is generally thickened, irregularly, from coincident periostitis. Syphilis may induce this change, especially in the long bones and in the bones of the skull. It is called **condensing ostitis** or **sclerosis**. It is said that simple closure of a large number of Haversian canals may lead to death of the affected bone. In syphilitic necrosis of the skull, the sequestrum is often very dense; it has probably been killed by degeneration and death of the inflammatory products in the bone around the sclerosed patch, and consequent destruction of the few vessels which entered it.

Nothing is commoner than to find rarefying and condensing ostitis combined. Osteoplastic periostitis and condensing ostitis frequently exist around carious patches: the surrounding bone is thus rendered thicker and denser. It may be that this less acute inflammatory process is coupled with true hyperplasia of the bony tissue.

NECROSIS.—It has already been shown that death of bone may follow, in several ways, different forms of inflammation, each leading, however, to destruction of vessels and arrest of nutrition.

This result may be brought about by injury stripping off the periosteum and breaking up the medulla; but the extreme rarity of necrosis, even in the most serious simple fracture, shows that injury alone, with such inflammation as it excites, is scarcely to be regarded as a cause. It may act indirectly, however, by preparing the nidus for septic (in compound fractures) and infective organisms. These constantly acting, and severe irritants so diminish the vitality that more or less extensive thrombosis, with death of the parts, ensues.

Suppuration beneath the periosteum and in the medulla are *the* causes of necrosis. This result is much commoner in compact than in cancellous tissue, owing to the greater ease with which exudations compress the vessels in the unyielding channels of the former. In rarefying and condensing ostitis (p. 457), death of the infiltration may produce necrosis, but in a less violent way.

The piece of dead bone is called a **sequestrum**: it is cast off by a process of caries (p. 23). It may be *total*—involving the whole thickness, *superficial*, or *central*—the last being much the rarest.

Considerable difficulty is often experienced in the removal of the sequestrum, especially if it be deeply seated. This difficulty is occasionally (*in central necrosis*) due to the persistence of a layer of the old bone enclosing the necrosed portion. Much more frequently, however, it is owing to the participation of the periosteum in the inflammatory process. The inflamed periosteum produces new bone; and the bony capsule thus formed encloses the sequestrum. Openings (*cloacæ*) exist in this capsule leading to the dead bone, and through these openings the inflammatory products are discharged. When the sequestrum is quite superficial, its removal is, of course, more readily effected.

There are two other morbid conditions of bone, which, although probably not coming within the category of inflammation, may be conveniently described in the present chapter—viz., **Mollities Ossium** and **Rickets**.

Mollities Ossium.

Mollities Ossium or Osteomalacia is a rare disease, occurring only in adults, and especially in pregnant women who have borne many

children. It is characterised by progressive decalcification of the bones, whilst the marrow increases steadily and becomes converted into a vascular round-celled structure. All bone is gradually absorbed, except a thin layer beneath the periosteum; so that in extreme cases the bones become mere shells. They are very light, easily cut with a knife, and bend or break readily. Early in the disease fractures unite. On section, in early stages, the cancellous spaces and Haversian canals are enlarged and full of a reddish, gelatinous substance, which at a later period may become yellow and fatty.

The nature of the disease is obscure. The pelvic deformity is of chief importance; the sacrum is pushed downwards by the weight of the body, and the acetabula upwards and inwards by the resistance of the femora, thus greatly shortening the two oblique diameters (p. 461).

Lactic acid has been found in the bone—the reaction of which is said to be acid—and in the urine. The latter usually contains excess of calcium salts which have been removed from the bone and excreted.

Rickets.

This disease of children is so frequent in the large towns of England that it has acquired on the Continent the name of the "English disease." It appears to be caused by defective hygienic conditions, especially by bad air and improper feeding. It is particularly common in children brought up by hand. It may probably be said that all conditions which materially interfere with the nutrition of a child aid in the causation of rickets; among these, the absence of *fresh* food ranks highest. Diets deficient in fats or in carbohydrates seem sometimes to be sufficient causes.

The disease is mainly characterised by changes affecting the growing tissues of bones, and is therefore most marked where growth is most active—viz., at the epiphyses of long, and at the margins of flat, bones. These changes produce undue thickness and softness, which, in their turn, lead to projections and curves, according to the pressure on the softened bones. The bone-lesions are accompanied by symptoms of general ill-health, and often by enlargement of the liver, spleen, and, less often, of the kidneys and lymphatic glands, due *chiefly* to increase of their interstitial connective-tissue.

The alteration in the bones may be briefly described as consisting in "an *increased preparation* for ossification, but an *incomplete performance* of the process" (Jenner). It will be remembered that if a section of

the end of a *healthy* growing long bone be examined, a straight line is seen where the white epiphyseal cartilage is adherent to the shaft, which here consists of loose cancellous tissue, with spaces filled with red marrow. Between the bone and the epiphysis is a blue, semi-translucent band about one millimètre broad with practically straight margins. Microscopically, the blue line is found to consist of the one or two layers of cartilage-cells which normally multiply and enlarge, forming the well-known oval groups among which ossification proceeds. The septa between these groups become very thin, and in the immediate neighbourhood of the shaft they calcify. A sudden transition from the cartilage-cells to those of the vascular red marrow is seen in these spaces. As soon as these spaces (*primary areolæ*) with calcified walls become occupied by the round-celled marrow, absorption begins, and adjacent spaces open into each other and form the larger *secondary areolæ*. On the walls of these, laminæ of bone are deposited, including osteoblasts in the lacunæ between them; and thus Haversian systems are gradually developed. The calcified cartilage-matrix is darker and more granular than the bone laid down by the medulla which gradually replaces it.

In a rickety bone, the blue transition-zone is much wider than normal, affecting several rows of cells; while its outlines, both towards the bone and towards the cartilage, are very irregular. The calcification of the matrix, in the formation of primary areolæ, occurs without any regularity. Hence patches of calcified matrix or of young bone may be found in the transition-zone, detached from the shaft; and oval collections of cartilage-cells may be seen among secondary areolæ full of red marrow. Speedy fusion of the primary into secondary areolæ occurs, but the deposit of laminæ of bone is insignificant.

Beneath the periosteum, an excess of osteoblasts form, and osteogenic fibres appear; but calcification is very backward. The medullary cavity is formed as usual by absorption from the centre, and thus the sound bone which was laid down before the onset of the disease, and which was distinguished from the rickety bone by its greater density and less opacity, is gradually removed. The bone, now consisting only of the soft rickety structure, yields more or less readily under pressure, or breaks under slight violence. The fracture, however, is often incomplete. As bending occurs, a buttress of bone is deposited along the concave side of the curve. This is often seen in the femur and tibia, giving the bones a flat, somewhat razor-like appearance.

The thickening of epiphyses, the displacements which occur about

the junction of shafts with epiphyses, the thickenings of the edges of cranial bones (*e.g.*, the parietals), and the abnormal curvatures of bones under pressure, are readily explained by conditions such as the above.

The process just described seems to be injurious to the subsequent growth of the epiphyses. They often join the shafts prematurely, dwarfed stature being the result.

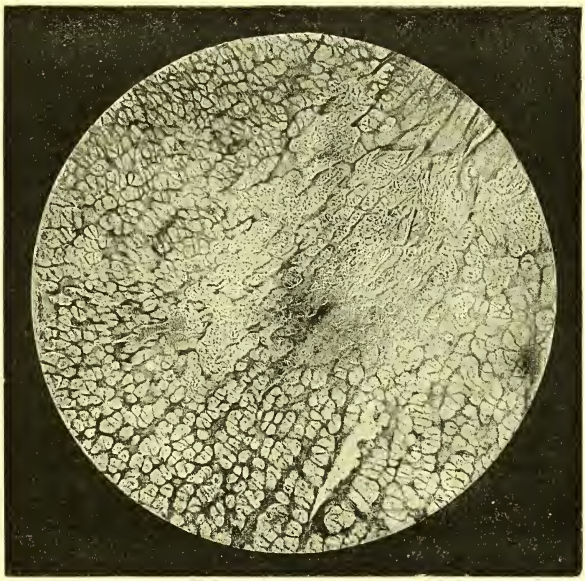


FIG. 158.—*Section of Rickety Radius.* Showing excessive multiplication of cartilage-cells and their arrangement in rows, and slight ossification of osteogenic fibres extending irregularly into the cartilage. (Mott.)

Among the most important of the deformities resulting from this disease is the **rickety pelvis**. There are two forms. The first shows *shortening of the conjugate diameter* only, and occurs in cases in which the child, being unable to walk, is kept lying down. The second resembles the *osteomalacic pelvis*, both in its shape and in the mechanism of its production, for it occurs in children who are able to walk about (p. 459).

CHAPTER XXVI.

INFLAMMATION OF BLOOD-VESSELS AND HEART.

Inflammation of Arteries.

It is generally taught that the middle and inner coats of arteries are non-vascular, the *vasa vasorum* not penetrating beyond the external coat; and that the intima is nourished by the blood in the lumen of the vessel. But Mott has shown that the vasa vasorum may enter the media, even in normal arteries, and has suggested that the apertures in the membrana fenestrata may allow fluids to pass from the vasa vasorum into the intima. In support of the view that the intima is not nourished solely by the blood within the lumen of the vessel, Mott has shown that it may persist round thrombi, which must have cut off that source of supply (Fig. 94, p. 225). Moreover, if it be true that the cells of the intima multiply and form anastomosing processes in organising thrombi, this conclusion receives additional support. It is quite certain that in chronic inflammation of the arteries, vasa vasorum frequently penetrate into the middle coat (Fig. 161).

As in other tissues, inflammation of arteries may be acute or chronic.

ACUTE ARTERITIS.—One form of acute arteritis especially affects the aorta. It leads to the formation of small, pearly, pinkish patches, slightly raised above the surface of the intima. Under the microscope, these are seen to be mainly due to a proliferation of the cells of the part.

Acute inflammation may also be produced by **injury,** as when a vessel is tied, twisted, or damaged by some irritant formed or impacted in its lumen (thrombus or embolus); or it may be the result of **extension** from surrounding parts. The changes in **traumatic arteritis** are described at p. 231, and the effects produced by simple thrombosis are similar. Plugging of an artery by a simple embolus causes a chronic inflammation; but infective emboli, as in cases of ulcerative endocarditis, are believed to produce acute infiltration and softening, and to be the chief cause of aneurysm in young people.

In **arteritis by extension**, the outer coat is first and chiefly

affected. If the process extends to the intima, the endothelium becomes detached, and thrombosis results. Thus destruction of vessels by ulceration does not cause hæmorrhage, unless the thrombus breaks down, as it may, if infected from a foul wound; this *septic arteritis* is the commonest cause of secondary hæmorrhage.

CHRONIC ENDARTERITIS.—Whilst the *acute* inflammations affect more or less generally the whole thickness of the artery,



FIG. 159.—*External Coat of Aorta in an Early Stage of Arteritis*, showing peri-arteritis and cell-infiltration from the vasa vasorum. The walls of the vasum vasorum seen in section are much thickened. It was a markedly syphilitic case. (Mott.)

the *chronic* inflammations affect primarily and sometimes solely the deeper layers of the intima—hence the term **chronic endarteritis.**

Chronic endarteritis is to some extent a senile degenerative change: its advent is accelerated by undue *mechanical strain*, by *syphilis*, and by chronic *alcoholism*. **Mechanical strain** is supposed to have a special influence in the production of that variety of chronic endarteritis which goes by the names of **arteritis deformans**, and **atheroma.** The proofs adduced are—the much greater frequency of these changes in the aortic than in the pulmonary system; their occurrence in the latter when the pressure is raised, as in mitral

obstruction ; their relative frequency in those systemic arteries which are most exposed to strain, especially the arch of the aorta ; and their presence in conditions accompanied by rise of blood-pressure. Thus athletes are very liable to the disease. It is, moreover, common in chronic Bright's disease, which is usually accompanied by a high-tension pulse. **Syphilis**, as a cause of endarteritis, has been considered in a preceding chapter (p. 432) ; and a special change in the

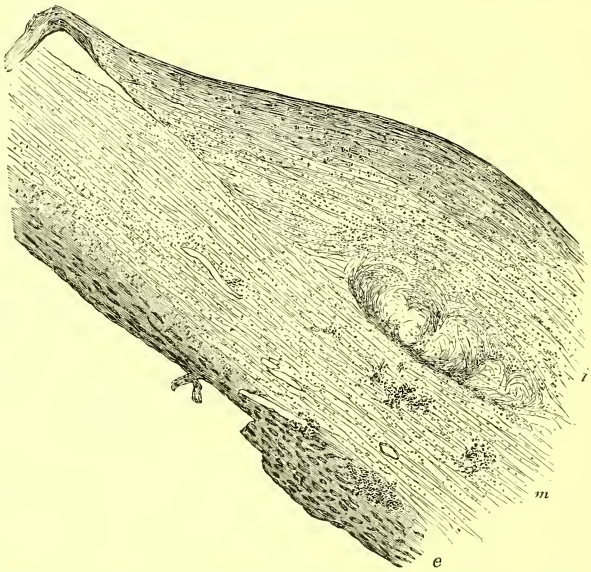


FIG. 160.—*Atheroma of the Aorta.* Showing the localised thickening of the inner coat, and the consequent bulging inwards of the vessel. Some of the new tissue has undergone fatty degeneration. There is also some thickening of the middle coat. *i.* Internal, *m.* middle, *e.* external coat of vessel. × 50. Reduced ½.

arteries, met with in chronic interstitial nephritis, will be described when that disease is discussed.

Atheroma affects chiefly the larger vessels of the trunk and limbs, and those at the base of the brain. It often forms rings round the mouths of branches leaving a main trunk ; but the whole circumference is not uniformly affected. It appears as slightly prominent yellowish patches, covered by a normal endothelium ; in fact, this and the superficial layers of the intima may, in the early stages, be stripped off, leaving the diseased tissue beneath. It thus contrasts strongly

with the superficial fatty patches, which result from fatty degeneration of the endothelial and sub-endothelial connective-tissue cells (p. 61).

In the earliest stage of the process, a greyish, semi-translucent mass of cells is found between the laminæ forming the deeper part of the intima. The origin of this is doubtful. It is probably due to a proliferation of the original tissue-cells; and this again may possibly be the result of the presence of some organism or other irritant. The new cells may develop into fibrous tissue, resulting in a dense fibroid plaque or a more diffuse thickening. More often, formation of fibroid tissue and fatty degeneration are found together (Fig. 160); or fatty degeneration and calcification may occur; or the fatty degeneration may lead to complete softening. In the latter case, a soft, yellowish, pultaceous material, consisting of fatty débris and cholesterin crystals, is found beneath the intima. This has been termed an *atheromatous abscess*. If the lining membrane perishes or is torn, the softened matters are carried away by the blood-stream, and an *atheromatous ulcer* is left. The middle and external coats become more or less infiltrated with new cells and the resulting fibrous tissue, especially in the aorta.

It is not uncommon to find the arch of the aorta so studded with small, thickly set, raised plaques that it looks somewhat like "crocodile skin." The plaques are yellow, and many of them are calcified. These calcareous plates may be quite bare, or covered by endothelium or a little fibrin: atheromatous abscesses and ulcers may also be present. The orifices and the branches of the coronary arteries are often narrowed by these changes; while the blood-supply to the heart is proportionately lessened, and the tendency to fatty degeneration of its muscular walls increased.

The cause of the fatty metamorphosis of the new cells is also in dispute. Köster and Kraft believe that a **mesarteritis**, or infiltration of the media, is the primary change in atheroma, and that conversion of the cell-infiltration into fibroid tissue causes constriction of the vasa vasorum, which send fine branches into the inflammatory patch in the intima: this consequently degenerates. But Orth and most authors deny that a mesarteritis either precedes or even accompanies the infiltration of the intima. Mott believes that fatty changes in the latter result from an endarteritis of the vasa vasorum, leading to progressive narrowing of their lumina: this is illustrated in Fig. 162.

It is obvious that atheromatous changes will greatly impair the

elasticity of a vessel, and render imperfect the circulation in the parts beyond. Moreover, the *inelastic* vessel-wall tends slowly to yield under the *constant* pressure to which it is subjected. General dilatation of the vessel results: when this is extreme, it is known as a **fusiform aneurysm**. When an atheromatous ulcer forms, the vessel is specially weakened at one spot, and a local dilatation or **sacculated aneurysm** may occur. When this has reached a certain size, the wall may rupture, and fatal hæmorrhage result. If the external coats have been uniformly strengthened by the formation of chronic inflammatory tissue in them, this result will be proportionately delayed. If an atheromatous abscess bursts before the tissues round its margin have been matted together



FIG. 161.—*Miliary Aneurysms on a Branch of the Middle Cerebral Artery*, from a case of cerebral hæmorrhage. They are not unlike birds' nests in a tree. (From a specimen by Dr. Mott.)

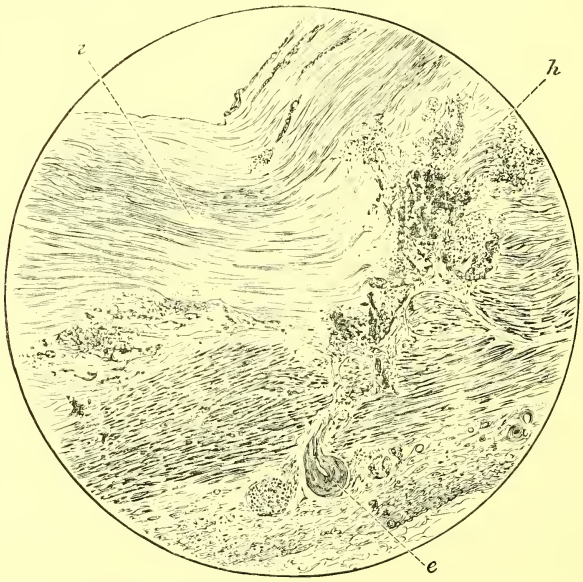


FIG. 162.—*Section of an Atheromatous Aorta:* the intima is much thickened (*i*); passing in from the externa through the media are vessels, about which hæmorrhage (*h*) has occurred; the lumina of the main trunks of these (*e*) in the externa are almost obliterated by an endarteritis. (Mott.)

by fibroid growth, the blood may find its way into the substance of the *media,* and making for itself a cavity between the coats of the vessel, form a **dissecting aneurysm**. This occurs only in the aorta and its largest branches. Ultimately the blood may burst through the *externa* into the surrounding tissues, or through the *intima* into the lumen of the vessel.

Inflammation of Veins.

Acute inflammatory processes are more frequent in veins than in arteries. In veins they are generally **secondary** to **thrombosis**, and are due to the irritating effect of the thrombus upon the coats of the vessel. These inflammations have already been described (p. 233). They are localised or spreading, according as the clot is simple or continued.

Other **causes** of phlebitis are violent **injury**, and **extension** of inflammation from adjacent tissues. Paget describes a recurrent gouty phlebitis especially common in the internal saphenous vein.

The structural changes closely resemble those in the arteries. In phlebitis from *injury* or from *extension,* the external and middle coats become infiltrated with cells, the vitality of the intima is subsequently impaired or lost, and thrombosis follows. In phlebitis from *thrombosis,* the intima suffers first.

Less commonly than in arteries, the veins, especially in the lower limb, may be studded internally with irregular calcified plaques.

When a clot undergoes infective puriform softening (Fig. 97, p. 235), the vein-wall becomes densely infiltrated with cells, and presents much the same appearance as when it becomes infiltrated by extension from a foul wound (*acute septic phlebitis*).

Varicose Veins.—In some persons especially predisposed, constant but comparatively slight increase of the venous pressure in the legs, scrotum, or rectum, will produce an irregular dilatation, lengthening, and tortuosity of the vessels in question. Portal obstruction will produce the same result in the veins of the hæmorrhoidal plexus apparently *without* any predisposition. Other veins are similarly, but less frequently, affected. The dilatation and other changes are accompanied by thickening of the walls, mainly due to the formation of chronic inflammatory fibroid tissue.

INFLAMMATION OF THE HEART.

Inflammatory processes in the heart may affect the substance of the organ or the endocardium. They are much more frequent in the last-named situation.

Inflammation of the Endocardium.

Endocarditis is for the most part limited to the valves of the heart, although it is occasionally found on the adjacent parts of the walls. After birth, the process is almost exclusively confined to the

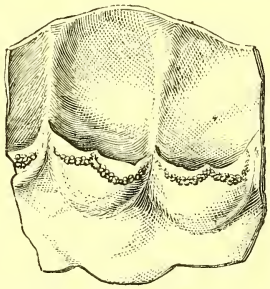


FIG. 163.—*Inflammation of Aortic Valves.* The earlier stage of the process. Showing the situation of the inflammatory granulations.

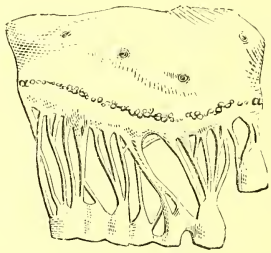


FIG. 164.—*Inflammation of Mitral Valve.* The earlier stage of the process. Valve seen from the auricular surface. Showing the situation of the inflammatory granulations.

left side of the organ, and in the great majority of cases, it commences in, and comparatively rarely extends beyond, the confines of the aortic and mitral valves and the corresponding orifices. But during fœtal life, endocarditis is as exclusively confined to the **right** side, giving rise to congenital lesions, and thus often interfering with the normal development of the organ. It is those portions of the valves which come into contact in the act of closure, and are thus *most exposed to friction,* which are especially involved, and in which the changes usually commence. Thus, in the aortic valves, it is the *convex* surface of the segments which is most liable to be affected. The change does not commence at the free edge of the segment, but along the little band of tissue which passes from the attached border to the corpus Arantii in the centre (Fig. 163). In the mitral valve, the auricular surface of

the segments at a little distance from the attachment of the chordæ tendineæ is first involved (Fig. 164). When portions of the endocardium, apart from the valves, are affected, it may sometimes be due to the irritation caused by the friction of vegetations or fibrinous clots, situated on the valves themselves; but it is probable that infection by organisms deposited from the original valve-lesion is the commoner cause (Fig. 165).

The histological changes accompanying endocarditis resemble those already described as occurring in arterial inflammation. The endocardium and the inner coat of an artery are very analogous in their structure, both being non-vascular, and consisting of a layer of connective-tissue with an internal endothelial covering. The inflammatory process may be *acute* or *chronic*.

ACUTE ENDOCARDITIS.—If the process be acute, the deeper layers of the endocardium become rapidly infiltrated with young cells, and as these increase in number, the intercellular substance becomes softened and destroyed, and thus is produced a soft tissue composed almost entirely of cells such as always results from inflammatory processes in connective-tissue. The new tissue, as it increases, projects through the superjacent endothelium in the form of minute granulations and vegetations upon the surface of the softened valve (see Figs. 163 and 164). The endothelial elements probably participate in the active process. This is the **papillary** form of the disease.

The above changes take place in an almost non-vascular tissue, and although there is more or less increase of vascularity in the external endocardial layers, where the capillaries are more numerous, there is rarely any redness or injection of the endocardium seen after death. The granulations, rough and bereft of endothelium, frequently induce sufficient thrombosis to provide them with fibrinous caps. These caps must not be confounded with the vegetations themselves (Fig. 166).

The results of this cellular infiltration vary. If the process be very intense, the new tissue may break down, and a loss of substance result —an endocardial **ulcer**. This usually takes place without any accumulation of cells sufficient to form an abscess, the new tissue simply undergoing rapid softening and disintegration; but, in rare cases, small quantities of pus are found in the deeper endocardial layers (**abscess**). The ulcer is irregularly defined, and its edges are usually swollen and thickened. The *ulceration* may lead to perforation

of the valve, or to a considerable destruction of its substance. Laceration or aneurysm of the valve may also ensue from the *pressure* exercised by the blood against the damaged tissue. Sometimes the ulcerative process extends so as to involve the cardiac substance. **Ulcerative endocarditis** is a grave affection, often giving rise to embolism, and sometimes to a pyæmic process. Fortunately, this

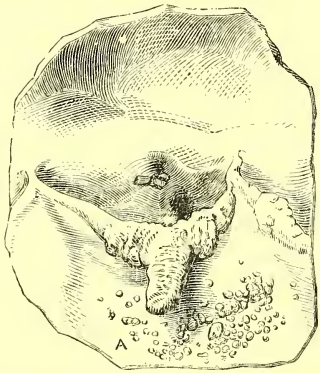


FIG. 165.—*Endocarditis due to Friction.* The drawing represents a long vegetation on one of the segments of the aortic valve, which by rubbing on the endocardium below has produced numerous inflammatory granulations (A).

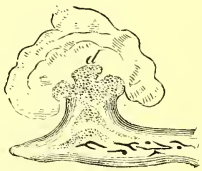


FIG. 166.—*Acute Endocarditis.* A granulation from the mitral valve, showing a fibrinous coagulum, upon the surface of the granulation (*d*). × 10. (Rindfleisch.)

ulcerative endocarditis is infrequent, the process usually being less acute.

When the inflammatory process is less intense, the granulating valves may adhere to each other, or to an inflamed patch on the wall of the heart. The new tissue becomes incompletely organised into a fibrillated structure, whilst it undergoes, in part, fatty and calcareous degeneration. These changes always produce permanent **thickening**, **rigidity**, and **shrinking** of the tissue with consequent *insufficiency* of the valves, or *stenosis* of the orifices, or both. The new tissue may continue to grow after the severity of the process has subsided, and thus are produced the vegetations and papillary excrescences on the valve, which are so commonly met with (see Fig. 165). These consist of a lowly organised tissue, which tends to undergo fatty and calcareous changes. The effect of these changes is, in general terms, to impair the

action of the heart. In some cases this is due to the difficulty in propelling blood through a constricted or partially obstructed opening, in others to the regurgitation of blood which may take place through orifices guarded only by damaged or imperfectly approximated valves (pp. 99, 212).

Ætiology. — Endocarditis occurs especially in acute rheumatism. It is an occasional complication of pyæmia, puerperal fever, gonorrhœal rheumatism, scarlatina, typhoid fever, and chronic Bright's disease. The papillary form is by far the commoner. The ulcerative may occur primarily, but as a rule supervenes upon the papillary or chronic forms.

The relation of endocarditis to the above diseases, and the course of the ulcerative form, suggest an infective origin. In ulcerative endocarditis many observers have found micrococci on the vegetations, and in the substance of the valves. The forms most frequently found are the staphylococcus pyogenes aureus, the streptococcus pyogenes, and less commonly Fränkel's diplococcus pneumoniæ and other forms of bacteria. These organisms have been cultivated, and the cultures inoculated. Ulcerative endocarditis has frequently been produced by a *very large* dose of the cultures. If the valves be previously injured, a much *smaller* dose suffices to produce a similar effect. Corresponding organisms are demonstrable in the secondary inflammations.

CHRONIC ENDOCARDITIS.—This may be the sequel of acute inflammation; or the process may, from its commencement, be chronic in its nature. Conditions of mechanical strain, such as lead to chronic endarteritis, are the most important causes of chronic inflammation of the endocardium. Hence chronic disease of the cardiac valves is frequently associated with atheroma of the arteries. The cell-infiltration is much less rapid and abundant than in the acute form; the intercellular substance consequently undergoes less softening and disintegration, and the new tissue has a much greater tendency to develop into a fibrillated structure. The result of these chronic processes is the production of a **fibroid thickening** of the endocardium, with more or less induration and contraction of the valves, narrowing of the orifices from the progressive adhesion (from their bases towards their apices) of adjacent cusps, and shortening and thickening of *chordæ tendineæ*. The effects on the circulation are the same as those produced by acute endocarditis. The new tissue sometimes forms papillary growths on the valves, which undergo partial fatty and calcareous changes (Fig. 165).

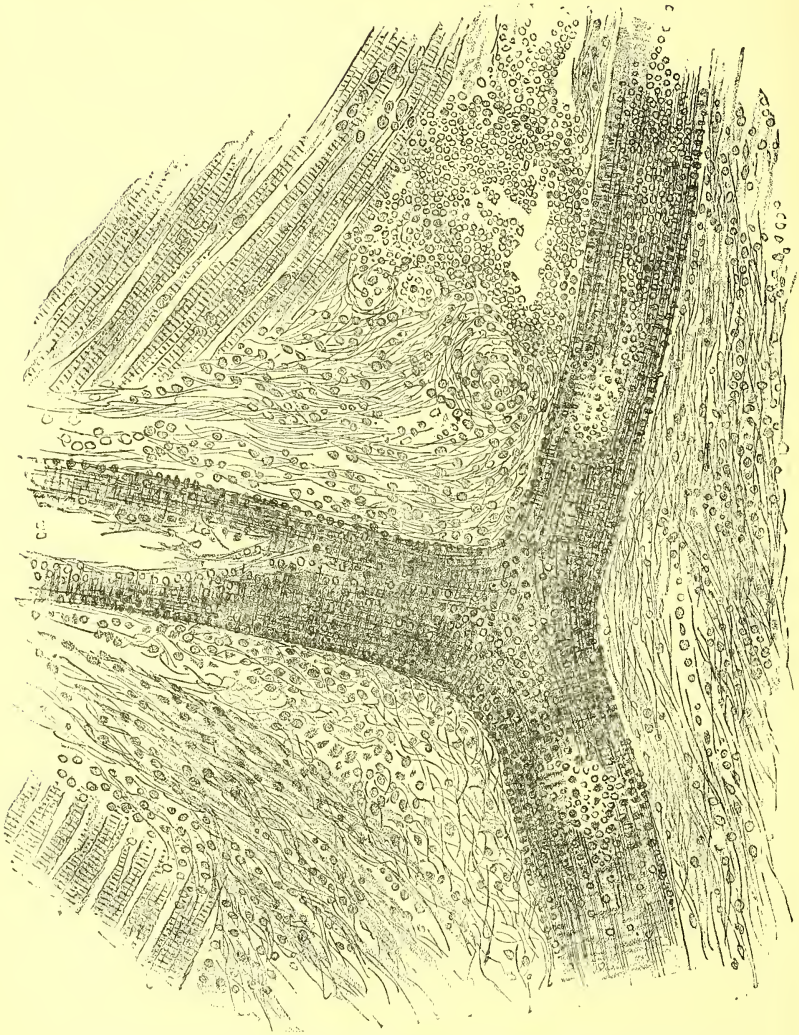


FIG. 167.—*Acute Rheumatic Myocarditis, associated with Endo- and Pericarditis.* To the naked eye, the myocardium was "fatty" only. The tissues around the artery, seen in longitudinal section, are infiltrated with leucocytes, and hæmorrhage has occurred in the upper part. A case of sudden death. (Mott.)*

* From "Myocarditis," by Dr. Bruce, in Keating's "Diseases of Children."

Inflammation of the Myocardium.

Myocarditis, or inflammation of the cardiac substance, is much less frequent than the preceding. Intense and concentrated inflammations, leading to the formation of abscess, probably occur only as the result of a pyæmic process. Less intense and more diffuse forms of cardiac inflammation are also not infrequently met with in association with pericarditis, and, less commonly, with endocarditis. Here the inflammatory process appears, by extension, to involve the immediately adjacent muscular layers of the organ, which are found infiltrated with small cells, the fibres themselves being softened and granular

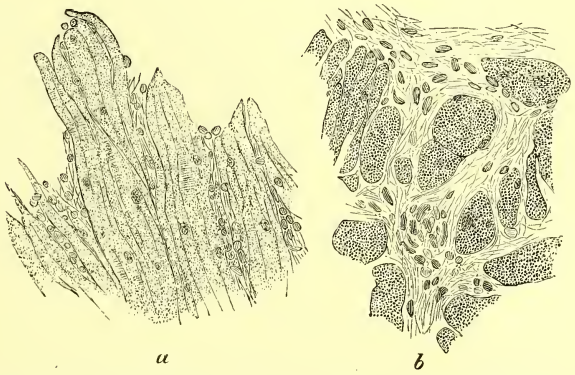


FIG. 168.—*Acute Myocarditis.* From a case of acute rheumatism. *a*. A thin section of the left ventricle made in the direction of the muscular fibres, showing the granular and swollen condition of the fibres, and the prominence of their nuclei. *b*. A transverse section, showing the cellular infiltration of the intermuscular tissue. × 200.

from degeneration, or clear and structureless from coagulation-necrosis.

In addition to the above, a *diffuse* form of myocarditis must be recognised in which the substance of the heart becomes more generally involved. In certain cases of acute rheumatism, the muscular tissue of the heart is found, after death, to have undergone the changes characteristic of *cloudy swelling* (p. 63). When examined microscopically, the nuclei of the fibres are often seen to be large and prominent, while small cells, in varying numbers, infiltrate the intermuscular tissue (Fig. 168). The change is most marked in the left ventricle, and it is usually associated with endocarditis or pericarditis (Fig. 167).

Fibroid Induration of the Heart.—This change is characterised by the presence of a fibrillated tissue between the muscular elements. The process commences in the intermuscular septa around the blood-vessels (Fig. 169). The affected parts may be so hard as to cut like a piece of tendon (Fig. 170).

The condition generally depends upon disease of the coronary arteries. It is usually, therefore, a localised change. Sometimes it occurs as a final result of embolism or thrombosis of a small artery, and merely consists of the scar-tissue which ultimately replaces the destroyed fibres (p. 247). At other times, the change may be

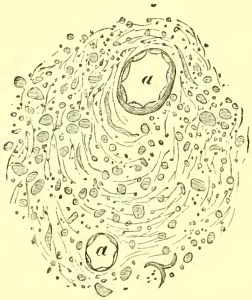


FIG. 169.—*Fibroid Induration of the Heart.* A section from the wall of the left ventricle, showing the small-celled growth in the intermuscular septa around the blood-vessels. *a.a.* Vessels. × 200.

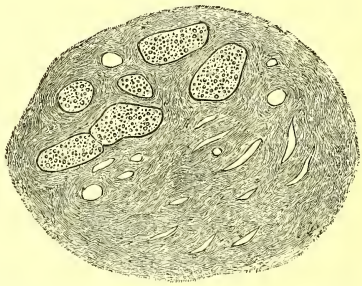


FIG. 170.—*Fibroid Induration of the Heart.* A section from left ventricle of the same heart as Fig. 169, showing a more advanced stage. The fibroid tissue surrounds the individual muscular fibres, which are undergoing fatty degeneration. × 200.

secondary to endarteritis and atrophy of the muscular fibres (see "Interstitial Nephritis," and p. 59).

Fibroid induration, like acute myocarditis, of the heart, appears in some cases to be induced by inflammatory processes commencing in the pericardium or endocardium. When secondary to pericarditis, the change is usually most advanced in the more external portions of the cardiac walls, and it commonly affects both the right and left ventricles. When, on the other hand, an endocarditis is the precursor of the indurative process, the change is more marked in the internal muscular layers, and, inasmuch as inflammatory processes in the endocardium occur almost exclusively in the left cardiac cavities, the left ventricle is principally involved. Even in these cases, it is probable

that the change follows atrophy of the fibres, which again is dependent on a deficient supply of blood. The change is by no means confined to those parts affected by the endocarditis. In other cases, the fibroid growth appears to be the result of syphilis (see "Syphilis").

Whatever the cause, the heart is usually enlarged, and the fatty degeneration of the muscular fibres is found outside the fibroid areas. Moreover, the function of the heart is materially impaired, and fibroid induration accordingly constitutes one of the gravest of all cardiac diseases.

Myomalacia cordis is the term applied to the presence of necrosed areas, which result from embolism or thrombosis of large branches of the coronary arteries.

CHAPTER XXVII.

INFLAMMATION OF LYMPHATIC STRUCTURES.

Inflammation of lymphatic structures usually results from their injury by substances conveyed to them through the lymphatic vessels. They include—**acute** and **chronic** inflammations, and the specific inflammations associated with **Typhoid Fever**. Each of these must be considered separately.

Acute Inflammation of Lymphatic Structures.

Examples of acute inflammation of lymphatic structures are furnished by the inflammation of the axillary glands which may follow a wound on the hand; of the inguinal glands, in a case of soft chancre; and of the lymphoid follicles of the intestine in inflammation of the intestinal mucous membrane.

Inflammation of lymphatic glands is almost always due to absorption of some *infective substance* from a primary focus of inflammation (diphtheritic, erysipelatous, scarlatinal, chancrous, &c.): micro-organisms, especially micrococci, have frequently been demonstrated in the inflamed glands. A gland affected by acute inflammation becomes intensely vascular, and the seat of free exudation. The escaping leucocytes accumulate in its tissues and sinuses, until all distinction

between medulla and cortex has disappeared; while the gland-substance is soft and pulpy, and often dotted with hæmorrhages. Leucocytes in the lymph coming from the primary focus are also detained in the gland.

Upon the removal of the injurious influence, the process may gradually subside, and the new elements undergo disintegration and absorption, the gland gradually returning to its normal condition (*resolution*).

In other cases the process goes on to *suppuration*, the trabeculæ are destroyed, many of the cells become disintegrated, and the loculi of the gland become filled with pus. This is usually associated with inflammation and suppuration of the surrounding connective-tissue. In the glands of a mucous membrane, the process gives rise to what is known as a *follicular abscess*. In still more acute cases, the inflammation may be truly hæmorrhagic.

Chronic Inflammation of Lymphatic Structures.

Chronic inflammations of lymphatic structures result from injuries which, while less severe, are more prolonged in their action than those which give rise to the acute form These chronic inflammatory processes differ still further from the acute, inasmuch as they lead to a gradually increasing development of the *reticular structure* of the gland. The reticulated network becomes thicker and more fibrous, its meshes becoming smaller and smaller; the lymph-cells diminish in number; and the gland becomes hard and fibrous (Fig. 171). Probably in these chronic cases, the cells of the gland-substance, and the flat connective-tissue cells covering the trabeculæ multiply, and assist in forming the infiltrating cells. Fatty patches are frequent in chronically inflamed glands.



FIG. 171.—*Chronic Inflammation of a Lymphatic Gland.* Showing the increase in the stroma, and the diminution in the number of the lymphoid cells. × 200.

Scrofulous Glands.—In those chronic inflammations of the lymphatic glands which occur in scrofulous subjects, and in which the glands tend to become caseous, the changes resemble those already described as characteristic of scrofulous inflammation (p. 420). The

accumulation of new cells is considerable ; there is but little tendency to absorption ; and many of the cells increase in size, and even form multinucleated elements. The gland thus becomes enlarged, soft and elastic in consistence, and of a uniform greyish-white colour. Retrogressive changes and caseation follow (p. 53). The caseous material may subsequently liquefy, or become infiltrated with calcareous particles. The great majority of caseous lymphatic glands are tuberculous, and the bacillus tuberculosis is found in them in small numbers.

Inflammation of Lymphatic Structures in Typhoid Fever.

Typhoid fever is an acute infective disease, generally attributed to the action of bacteria (p. 359).

The ordinary duration of the fever is three or four weeks, and the temperature as a rule both rises and falls (*lysis*) gradually. The most characteristic lesions are found in *lymphoid tissue*—especially the solitary and agminated follicles of the intestine, the corresponding lymphatic glands, the spleen, and sometimes the red marrow. The *intestinal* lesions are the most constant, and their various stages so often correspond with definite clinical conditions, that we can, not infrequently, judge of the state of the intestine from the symptoms and the day of the disease.

Many believe that infection occurs from the intestine, and that the intestinal lesions are points of inoculation ; but there is no *constant* relationship between the severity of the intestinal ulceration and the severity of the symptoms. Patients with extensive ulceration are sometimes able to attend to their business until suddenly struck down by perforation of the intestine or by hæmorrhage from an ulcerated vessel.

The pathology and morbid anatomy of typhoid fever include more than the lesions of the above-mentioned organs. First, there is the evidence of general poisoning in the shape of the continued *fever*, which may assume a septic type, and even be accompanied by septic abscesses, probably resulting from a mixed infection. Naturally, in so long a fever, *cloudy swelling* (p. 63) of organs is marked. Not uncommonly, waxy degeneration of muscle (p. 68) is found. Endocarditis is rare. Ulceration of the larynx, especially about the epiglottis, is occasionally present. This may lead to œdema of the glottis or to necrosis of the cartilages. *Bronchitis* is usual, and broncho-

pneumonia may supervene; œdema of the lungs is common in fatal cases; and lobar-pneumonia is a rather frequent complication in some epidemics.

The Spleen.—In the spleen, the change resembles that which occurs in many of the acute febrile diseases, although it reaches its maximum in typhoid fever; but it may be absent, especially in the older class of patients. The splenic tissue becomes exceedingly vascular; the lymphatic elements increase rapidly in number, so that the organ often attains two or three times its natural size; and the capsule becomes tense. The consistence is fairly firm during the first week; but softening occurs in the second or third. On section the organ is dark red and opaque-looking, and the Malpighian bodies are often prominent and enlarged. Many of the new elements are supposed to enter the blood, and thus cause slight leucocytosis (p. 203); but the increase is generally said to be mainly of the *multinucleated* leucocytes, not of the *lymphocytes*, or their progeny, the *mononucleated* leucocytes (p. 297). Large corpuscles, containing normal or altered red corpuscles, may be numerous, and similar cells have been found in the blood. As the fever subsides (fourth week), the hyperæmia diminishes, and many of the new elements undergo disintegration and absorption: thus the organ regains its normal characters and dimensions.

The Intestine.—The most characteristic changes in typhoid fever take place in the solitary glands and Peyer's patches. In most cases the process is limited to those in the ileum and cæcum; and those glands are always most affected which are situated nearest to the ileo-cæcal valve. The cæcum is involved in one-third of the cases: ulcers may be present even in the rectum, but in the great majority of cases they are not found *below* the ascending colon. It is, moreover, unusual to find ulcers higher than nine feet *above* the valve, but they *may* extend even into the upper part of the duodenum.

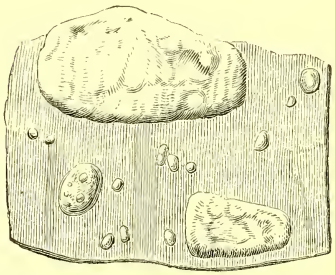


FIG. 172.—*Swelling of Peyer's Patches and Solitary Glands of the Intestine*, as seen in typhoid fever.

The first change observed is a hyperæmia and cell-infiltration of the glands. Many of the cells increase considerably in size, and multinucleated forms are especially common. Both Peyer's patches and the

solitary glands thus become considerably enlarged and prominent, and stand up, as sharply circumscribed areas, above the surface of the intestine (Fig. 172). Sometimes they slightly overlap the adjoining mucous membrane, and are surrounded by a hyperæmic zone. They are of a greyish-white or pale red colour, and of a soft, brain-like consistence—the larger the size, the paler the colour. The surrounding mucous membrane is also exceedingly vascular, and is the seat of an acute general catarrh, which is most pronounced before the glands swell. The cellular infiltration, in many parts, rapidly extends beyond the confines of the glands into the immediately surrounding and subjacent tissues, and in some cases even into the muscular and serous coats. This stage ends in the first half of the second week of the disease.

The process now passes into the second stage—that of the death and disintegration of the newly formed tissue. Many of the enlarged glands subside, the new elements become fatty and are absorbed, and the inflammation thus undergoes a gradual process of **resolution**. But in other glands the intensity of the virus—possibly typhotoxine or some other bacterial product (p. 362)—causes death of the inflamed lymphoid tissue. The necrosed tissues then separate. If a few scattered follicles in each patch have alone been destroyed, only small sloughs will be formed; and after the separation of these, the Peyer's patches thus affected will assume a peculiar reticulated appearance. If on the other hand, as is most usual, the entire lymphoid mass is killed, this will separate as one or more large sloughs, and the typical **typhoid ulcer** will be formed (Fig. 173). Resolution or necrosis *begins* during the latter half of the second week. In the case of necrosis, the sloughs *separate* towards the end of the third, or during the beginning of the fourth week. This is the period of danger in which either severe **hæmorrhage**, or **perforation** into the peritoneal cavity may take place.

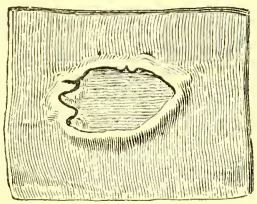


FIG. 173.—*A Typhoid Ulcer of the Intestine.*

Although, as already stated, the cell-infiltration may extend beyond the confines of the glands, this is rarely the case with the ulceration. The peripheral infiltration undergoes resolution, and hence the ulcers have the same configuration as the original glands—those originating from the patches being oval, with their long diameters in the direction of the gut; and those originating in the solitary glands being spherical

in shape, like those from partial sloughing of a patch. In rare cases, when there is much infiltration of the surrounding mucous membrane, the ulceration may extend slightly beyond the confines of the glands. An ulcer from a single Peyer's patch may be five inches long; and the blending of ulcerated patches and follicles in the neighbourhood of the ileo-cæcal valve, may affect so large an area, that this part of the intestine may seem to have lost almost all its mucous membrane.

With the sloughing and disintegration of the new tissue, the process of infiltration ceases, and hence there is no induration or thickening of the base or edges of the ulcer. The base is smooth, and is usually formed of the submucous or muscular coat of the intestine. The edges are usually thin and undermined, and consist of a well-defined fringe of congested mucous membrane (Fig. 174). This is best seen when the gut is floated in water. In some cases, especially where



FIG. 174.—*A Typhoid Ulcer of the Intestine* (*diagrammatic*). Showing the undermined edges of the ulcer and the slough still adherent. *a*. Epithelial lining. *b*. Submucous tissue. *c*. Muscular coat. *d*. Peritoneum.

there is surrounding infiltration, the edges are firm and thick. In others, again, the sloughing is deeper, and extends through the muscular layer to the peritoneum. This may either slough or give way under some muscular effort, either of the bowel, when stimulated by improper food, or of the abdominal muscles, when the patient is allowed to use them strongly. The perforation is generally small. As a rule *diffuse* peritonitis (purulent) results: rarely, adhesions form and localise the inflammation. Peritonitis may also occur by simple extension from the gut, from an inflamed gland, or from a splenic abscess. Hæmorrhage may occur from any vessel divided during the separation of the slough. It is due either to insufficient plugging by thrombosis or to mechanical displacement of the thrombus after it is formed.

The third stage of the process is that of cicatrisation, which usually begins in the fourth week. This takes place by the resolution of the peripheral infiltration, the approximation and union of the undermined edges with the floor of the ulcer, and the gradual formation from the margin of an epithelial covering. The gland-structure is not

regenerated. The resulting cicatrix is slightly depressed and less vascular than the surrounding mucous membrane. It is pigmented either uniformly, or only round the margin. There is no puckering or diminution in the calibre of the gut. In some cases, however, cicatrisation does not take place so readily, and the floor of the ulcer becomes the seat of a **secondary** ulceration. This may take place after the general disease has run its course, or during a relapse. Profuse hæmorrhage and perforation more commonly result from the secondary ulceration than from the primary sloughing of the glands. Only one ulcer may be affected by this secondary process, the rest having either healed or being in a fair way to become so.

Comparison between Typhoid and Tubercular Ulceration.—From the foregoing descriptions of typhoid and tubercular (p. 408) ulceration of the intestine, it will be noted that these two conditions have one important character in common—viz., the uniformity with which both arise in the lymphoid tissue. Hence in both cases the ulcers are most marked in the ileum opposite the mesenteric attachment, and may be limited to the Peyer's patches and the solitary glands. There are, however, two characters possessed by tubercular ulcers which generally suffice to distinguish them from typhoid ulcers. The first is the much greater tendency of tubercle to spread by means of the vessels, and the second is the presence of outlying tubercles which invariably precede the advance of the ulceration. Thus, the typhoid ulcer, remaining limited to Peyer's patches, has its long axis *parallel* to that of the intestine. On the other hand, the tubercular ulcer, often spreading transversely with the vessels before it has involved more than half the patch, has its long axis *at right angles* to that of the intestine, round which it may form a band. Again, as the slough separates, the floor of the typhoid ulcer tends to become cleaner and smoother, and its edges thinner and more undermined. On the other hand, the floor, base, edges, and adjacent peritoneum are, in the case of the tubercular ulcer, always thick and irregular from the presence of developing and degenerating tubercles.

The Mesenteric Glands.—The change in the mesenteric glands is probably secondary to that in the intestine. These glands become the seat of an acute cellular infiltration, and are enlarged, soft, and vascular. Usually, like the spleen and many of the glands in the intestine, they undergo a gradual process of resolution. In rare cases, however, the capsule of the gland is destroyed, and the softened matters may escape into the peritoneal cavity and so cause peritonitis.

The enlarged glands may also become caseous and subsequently calcified.

The Marrow.—Ponfick has shown that in typhoid fever the marrow of bones, like the splenic *pulp*, may contain large cells, in which may be as many as twenty-five red corpuscles: these break down, and in the convalescent stage the large cells only contain pigment.

CHAPTER XXVIII.

INFLAMMATION OF MUCOUS AND SEROUS MEMBRANES.

Mucous Membranes.

Inflammations of mucous membranes are divided into **catarrhal**, **croupous**, and **diphtheritic**.

CATARRHAL INFLAMMATION.—This may, according to its intensity, be serous, mucous, muco-purulent, or purulent. Acute cases begin with redness, slight swelling, and abnormal dryness of the mucous membrane, some tenderness of the part, perhaps even pain. These changes are followed by exudation from the surface, and the symptoms are then, as a rule, relieved. In chronic cases, the early changes are less marked, the exudation being usually the first thing noted. *Post-mortem*, no hyperæmia can generally be found, and the membrane may look even paler than natural; but, after repeated inflammation of any intensity, more or less dark-grey pigmentation, from extravasated blood, will, in most situations, bear evidence of the former attacks (p. 88). These appearances can be readily seen in an inflamed bladder from a case of stricture of the urethra, or enlarged prostate.

Serous Catarrh.—Free serous effusion occurs from the vessels and escapes upon the surface: this is often seen in the early stage of colds in the head.

Mucous Catarrh is characterised mainly by increased production of mucus, which escapes with the serous exudation, or remains adherent to the surface, as is often seen in chronic pharyngitis. Sometimes the sero-mucous discharge is tolerably clear, at others, it is more or less opaque: in the former case, only a moderate number of

cell-forms are present; in the latter, many. The cells are either escaped leucocytes, or desquamated epithelial elements.

Purulent Catarrh.—If the inflammation be more intense, the escape of leucocytes will be still greater; and the secretion will therefore be purulent. The more closely the exudation resembles true pus, the less mucus and desquamated epithelium will it contain. An intermediate **muco-purulent** stage usually occurs.

A section through a mucous membrane thus affected (Fig. 175) shows desquamation of the superficial epithelial cells, which are swollen, and often contain broods of young cells. Leucocytes lie here and there between the deeper cells, in which evidence of multiplica-

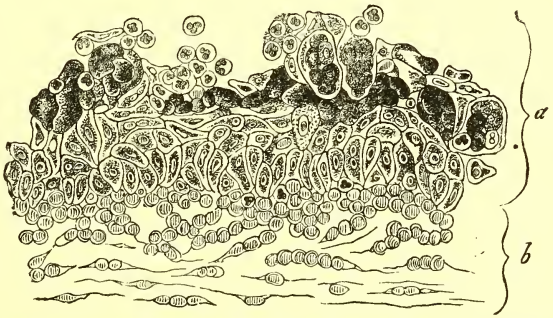


FIG. 175.—*Catarrhal Inflammation of the Conjunctiva.* *a*. Epithelium. *b*. Infiltrated sub-epithelial connective-tissue. Showing the desquamation of the epithelium, and the young elements within the epithelial cells. (Rindfleisch.)

tion will be found. The basement membrane becomes œdematous, and the mucosa is swollen. The swelling is at first mainly due to the leucocytes and exuded fluid; later on, if the process has been sufficiently prolonged, to the resulting fibroid tissue.

Simultaneously, all *lymphoid structures* in the mucous membrane are affected. The lymph-follicles swell, and their contents may soften and form minute abscesses, which burst and leave the small ulcers (follicular) so often seen in catarrhal conditions of the intestines and pharynx. The ulceration in some cases extends beyond the confines of the follicle. The proper *glandular structures* also may become involved. Their epithelium multiplies, and their lumen becomes choked with the products. The glands may subsequently atrophy: this is seen in catarrh of the stomach.

The acute process may quickly subside, or it may become chronic. In the latter case the hyperæmia diminishes, but the escape of leucocytes and the multiplication of the epithelial elements continue; while the sub-epithelial tissue becomes more extensively infiltrated with small cells.

In the case of the stomach and upper part of the duodenum, *follicular ulcers*, unattended by any general inflammation, may spread, and form the "acute perforating ulcers" which frequently occur in these situations. Their extension, in this way, probably depends on some interference with the local blood-supply; on errors in the composition of the blood; on an increased percentage of free hydrochloric acid in the gastric juice; or on any combination of these factors.

Chronic catarrhal inflammations of mucous membranes differ from the acute, inasmuch as the glands, at first enlarged, often undergo atrophy, while the sub-epithelial connective-tissue is more often and more extensively infiltrated with small cells, which ultimately form an imperfectly fibrillated structure. Here and there the contraction of this new tissue may lead to the formation of small retention-cysts (p. 193). These changes in the sub-epithelial connective-tissue are usually accompanied by enlargement of the lymphoid structures—an enlargement which sometimes gives to the membrane a nodular or granular appearance. This is well seen in the pharynx (*follicular pharyngitis*). The enlarged lymphoid structures may ulcerate, and constitute the starting-point of an infective process (p. 399). In chronic catarrh, the muscular and elastic tissues, although some distance from the surface, may be so far weakened, that when considerable pressure is put upon them—as in the cough of chronic bronchitis—they may give way, and permit dilatation of the tubes they surround. In some situations, as in the stomach and intestine, the membrane often becomes pigmented, and the walls thinned.

CROUPOUS AND DIPHTHERITIC INFLAMMATION.—These terms are applied to those inflammations of mucous membranes and raw surfaces which lead to the production of a so-called **false membrane**—such as is seen in diphtheria. The formation of this fibrinous layer upon the surface of the membrane is quite characteristic, and at once distinguishes this form of inflammation from a simple catarrhal process. On mucous surfaces, the membrane may exist in little patches or may cover a large area. It is

usually of a yellowish or greyish-white colour, and in consistence varies from a firm and tough to a soft pultaceous material: it may be deeply blood-stained. It is more or less easily separable from the subjacent tissue, and when removed, carries at least the surface-epithelium with it. In thickness it may vary considerably in different parts. The two words—croupous and diphtheritic—owe their origin to the belief, still held by some, that there is an idiopathic membranous inflammation of the larynx (croup) distinct from diphtheria. The adjectives are often used as synonymous, but many speak of a membrane as **croupous**, when it involves no more than the *epithelium* of a mucous membrane, and as **diphtheritic**, when it involves the whole *mucosa*. These differences in the depth of the tissue involved are probably due to variations in the intensity of the process; and, according to Cohnheim, the process is more likely to be superficial in those situations where a distinct basement membrane exists—as in the pharynx and respiratory tract—than in those where this is not the case—as in the intestines and conjunctiva. A false membrane, superficial to the basement membrane, is much more easily detached than one which involves this structure.

Others limit the term **croupous** to false membranes formed chiefly of *coagulated fibrin*, whilst **diphtheritic** is applied to those consisting of tissues which have undergone *coagulation-necrosis* (p. 22). This division renders "croupous" equivalent to "fibrinous." It must be remembered, however, that the two processes—formation of fibrin and coagulation-necrosis of cells—are closely allied, and that one may succeed the other in the same case.

The relative rarity of fibrinous inflammations of mucous, as compared with serous, membranes led Weigert to investigate the reason of the difference. He found that inflammatory exudations from mucous membranes coagulated as soon as the epithelium was destroyed, and he started the hypothesis that *living* epithelium, like endothelium, prevents the formation of fibrin.

Now, an injury which causes destruction of epithelium must be more intense than one which does not; and it is likely that the exudation in the former case will be more highly fibrinous than in the latter. Thus, in a case of true diphtheria, a patch of epithelium and more or less of the subjacent tissue are killed by the irritant, and undergo coagulation-necrosis; and, if the false membrane thus formed be removed, a fresh one will appear, which, unless the destruction of tissue extends, can hardly consist of anything but coagulated fibrin.

The two kinds of membrane differ microscopically. The *fibrinous* has the appearance of "lymph"—a network of fibrin, containing in its meshes a greater or less number of leucocytes, desquamated epithelial cells, and débris: it is easily stripped off. The *diphtheritic* membrane is separated less easily, and, if deep, only with great difficulty. Superficially, it closely resembles the croupous membrane, but the deeper parts consist of much swollen, homogeneous cells, from which the nuclei have disappeared. In advancing cases, there is no sharp line between the coagulated and the living tissue-elements. These membranes resist acetic acid much longer than do the simple fibrinous ones.

False membranes can probably form upon any mucous surface. The apparent causes are very varied. Such membranes are found (1) on the tonsils, larynx, and other parts, in true diphtheria, or as a result of scalds and the application of caustic chemicals; (2) in the bladder after parturition (when a complete cast may be expelled), and in the most acute cystitis; (3) in the vermiform appendix, sometimes from the irritation of a concretion; (4) in the lower part of the large intestine in dysentery; and (5) in the air-tubes in plastic bronchitis. It may be noted here that false membranes sometimes form upon granulating wounds, and it is held by some that there is no real distinction between such cases and those of true diphtheria of wounds, and of hospital gangrene. It seems most probable, however, that there is an ætiological difference, for false membrane on granulations may be induced by merely blistering the surface.

Although the above facts show that false membranes may result from the action of simple irritants, the great majority met with in Man are due to **infective** poisons—*e.g.*, diphtheria, diphtheritic conjunctivitis, epidemic dysentery—all highly contagious. Organisms are found in almost all cases. The ætiology of diphtheria has already been considered (p. 363).

Dysentery.

The inflammatory processes occurring in dysentery are for the most part limited to the large intestine, although the ileum is also occasionally involved. The inflammation is always most marked in the rectum and descending colon, and it may be stated generally that it is characterised by ulceration and sloughing of the mucous membrane, though the inflammation may be mainly of the catarrhal, croupous or suppurative variety.

The intestinal changes vary considerably, according to the intensity of the inflammatory process. In the milder forms of the disease, the changes are most marked on the summits of the folds of the mucous membrane. These are found covered with a greyish-white layer of fibrinous-looking material, which, when scraped off, leaves a superficial loss of substance. The mucous membrane, generally, is hyperæmic and softened. The submucous tissue also is infiltrated with inflammatory products, and the solitary glands are enlarged and prominent.

When the process is more severe, the submucous tissue becomes more extensively involved ; and the superficial layer of fibrinous material extends over wider areas, and implicates more deeply the mucous membrane. The thickening of the intestinal wall, however, is much greater in some parts than in others, so that projections are produced upon the inner surface of the intestine, corresponding with those parts which are the most affected. The enlarged solitary glands usually slough, and so give rise to circular ulcers, which rapidly increase. When the process has reached this stage, the muscular and serous coats are implicated, the latter being covered with layers of fibrin which form adhesions with adjacent parts. The intestine is much dilated, and contains blood and disintegrating inflammatory products.

In the most severe forms of the disease, the necrosis is more extensive. According to Rokitansky, large portions of the mucous membrane are converted into black rotten sloughs. The submucous tissue is infiltrated with dark blood and serum, but subsequently it becomes the seat of a reactive suppurative inflammation, by means of which the necrosed portions of tissue are removed.

If death does not occur, and if the inflammatory process subsides, the ulcers may gradually heal. When the loss of substance has not been considerable, the edges of the ulcers may, by the contraction of the submucous tissue, become completely approximated. More commonly, however, the loss of substance is so great that portions of the membrane are left, consisting simply of connective-tissue.

When the inflammatory process becomes chronic, the changes in the submucous connective-tissue become more marked, and the new fibroid growth gives rise to considerable thickening and induration of the intestinal wall, and to more or less contraction and narrowing of the cavity. Sometimes it forms fibrous bands, which project into the gut. Abscesses and fistulous passages occasionally occur in the thickened intestinal wall.

The **ætiology** of dysentery is unknown. By some, it is attributed to the presence of amœbæ (amœba coli); by others, to bacteria.

Extensive ulceration of the colon is sometimes met with apart from true dysentery. In these cases, the internal surface of the colon is made up of sinuous islets of mucous membrane, with thickened submucous tissue. These islets are separated by large areas of exposed muscular wall, from which all trace of mucous membrane has disappeared. Any solitary glands, present in the islets, are unaffected.

Serous Membranes.

Inflammatory processes in serous membranes vary in their intensity, and in the amount and character of the effusion.

As in mucous membranes, the process commences with hyperæmia. Exudation, both of fluid and of corpuscles, into the serous cavity quickly

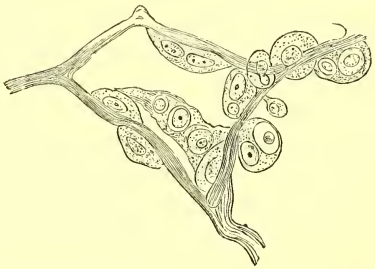


FIG. 176.—*Inflamed Epiploon of a Rabbit.* Showing changes in the endothelium. × 250. (Cornil and Ranvier.)

follows, with proliferation and desquamation of the endothelial cells (Fig. 176).

In the meantime the surface of the membrane has lost its polish. This is due to the presence of the new cells and a little fibrin on the surface. The moistening of the surface with the albuminous exudation renders it "greasy." As the inflammation goes on, the surface becomes opaque, roughened, and exceedingly vascular: it is now covered with a thick fibrinous layer, whilst more or less liquid transudes into its cavity. The coagulable material, which exudes from the vessels, forms a soft, elastic, membranous, or reticulated investment, enclosing in its meshes numerous small cells. Sometimes this glues the two surfaces of membrane together, collecting especially where pressure is least—viz.,

in the angles between contiguous coils of intestine, where the hyperæmia is also most marked. If the surfaces are separated by liquid effusion, the coagulable exudation forms a slightly adherent layer (Fig. 177). The exuded liquid varies considerably in amount, and is always turbid, thus differing from non-inflammatory effusions. It contains flakes and masses of coagulated fibrin, and innumerable cells, the latter being, in the earliest stages of the process, almost entirely emigrants.

The nature of the subsequent changes will depend upon the intensity of the inflammation, and upon the amount of liquid exuded into the serous cavity. If the inflammatory process subsides, and the liquid exuded is not sufficient to prevent the two surfaces of the membrane

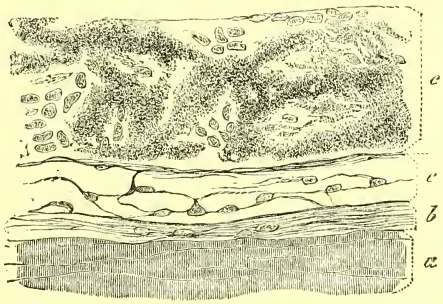


FIG. 177.—*Inflammation of the Diaphragmatic Pleura.* Showing the adherent fibrinous layer. *a.* Muscular coat of diaphragm. *b.* Subserous tissue. *c.* Serous membrane. *e.* Fibrinous layer. × 400. (Rindfleisch.)

from coming into contact, they grow together and form an **adhesion**. This constitutes the so-called **adhesive inflammation**. The union is effected by the formation of connective-tissue (p. 276). This is by far the most frequent form of inflammation of serous membranes. The process is precisely similar to that which takes place in the union of an incised wound. It is probable also that, in some cases, union may take place, without the intervention of any fibrinous layer, by the formation and growing together of irregular papillary outgrowths from the sub-endothelial tissue.

If, however, the inflammatory process is severe, or the surfaces of the membrane are separated by a large quantity of liquid effusion, organisation and adhesion cannot be effected. If a large quantity of liquid exists in the serous cavity, the removal of this becomes necessary before

union can take place. If the intensity of the irritant is considerable and its action prolonged, union is prevented by the formation of pus. These two conditions must be considered separately.

1. The existence of a large amount of effusion prevents approximation, and therefore adhesion, of the serous surfaces, and before this can be effected, absorption of the liquid becomes necessary. The presence of the liquid itself, however, interferes with its absorption (p. 288). The removal of some of the liquid by artificial means consequently facilitates absorption of the remainder. When the process is protracted, the sub-endothelial connective-tissue becomes involved, and infiltrated with small cells. A richly vascular granulation-tissue is formed beneath the layer of proliferating endothelium, which gradually disappears. As the liquid is absorbed, the two surfaces come into contact and grow together as in the previous case, the new vessels becoming gradually obliterated.

2. If the inflammatory process does not subside, or if from its commencement it is of considerable intensity, it may be attended by the formation of large quantities of pus. In this case, the exudation of blood-corpuscles is so considerable that the young elements exist in large enough numbers to give to the exuded liquids a purulent character. The condition is then termed **empyema**. As the connective-tissue becomes involved, a granulation-tissue is formed; and this may continue to generate pus like an ordinary granulating wound. If the pus be removed and the cavity drained, suppuration will gradually cease, the granulation-tissue develop into a fibrous structure, and the union of the opposing surfaces take place. The serous membrane becomes greatly thickened, and the new tissue undergoes considerable contraction in the process of its organisation, producing more or less retraction of the chest-wall.

Calcareous plaques of considerable size may develop in an adherent parietal pleura.

CHAPTER XXIX.

INFLAMMATION OF THE LIVER.

Inflammatory processes in the liver comprise — **perihepatitis**, **abscess**, and **cirrhosis**.

Perihepatitis.

Inflammation of the capsule of the liver, leading to more or less thickening, and often to adhesions with adjacent parts, is met with under various circumstances. Its most common causes are—the chronic peritonitis of Bright's disease, chronic alcoholism, and syphilis. The changes are usually slight and of but little pathological import.

In some cases, however, especially in cases of chronic peritonitis, the process is more extensive and leads to marked interference with the functions of, and circulation in, the liver. The whole capsule becomes considerably thickened and gradually contracts, thus causing compression of the organ, which assumes a globular form. The portal circulation is often interfered with by the squeezing process, and ascites, with other symptoms of portal obstruction, may result. The liver itself, with the exception of some atrophy and fatty degeneration of its cells, may show no changes; but sometimes it is intersected, and even divided into lobe-like masses, by bands of fibrous tissue passing inwards from the capsule. This suggests syphilis as the cause (p. 434).

Hepatic Abscess.

Acute inflammation of the liver leads to the formation of **abscess**. The abscess may be **single** or **multiple**. The latter are usually small, but a solitary abscess may attain an enormous size.

Multiple abscesses are most frequently due to pyæmia, or to some inflammatory lesion in connection with the portal system—such as dysentery. In these cases, the abscesses are due to infective embolism of branches of the portal vein. External violence and inflammation of the bile-ducts from gall-stones, are other causes of suppurative hepatitis.

The **solitary** or **tropical** abscess is supposed by many to be secondary to some inflammation of the portal viscera. It is known to

be often associated with dysentery. It is thought by many to be due to a primary hepatitis, excited by some unknown irritant, and doubtless cases often occur in which no intestinal ulcer or other obvious cause is discoverable. The pathology of this disease is, at present, obscure.

Cirrhosis of the Liver.

Chronic inflammation of the liver constitutes the condition known as **Cirrhosis**. This is characterised by a gradual increase in the connective-tissue of the organ, and by the subsequent atrophy of



FIG. 178.—*Cirrhosis of the Liver.*—Showing the growth of connective-tissue between the hepatic lobules. *a*. Lobules. *b*. New growth of interlobular connective-tissue. × 16.

the liver-cells, so that, when examined with a low magnifying power, the lobules are seen to be separated by new interstitial growth (Fig. 178).

HISTOLOGY.—The process, like that of chronic inflammation in other organs, consists essentially in a cellular infiltration of the interlobular connective-tissue of the liver, and in the subsequent development of a more or less highly organised fibroid structure—the number of cells being proportionate to the activity of the process. The new tissue is supplied with new blood-vessels, derived from branches of the hepatic artery.

In addition to this cellular infiltration of the interlobular connective-tissue, a proliferation of the bile-ducts is supposed to occur frequently

in some forms of cirrhosis. Charcot believed that in these cases there existed some obstruction of the ducts—the so-called "Biliary Cirrhosis." Other observers, however, state that the columns of cubical cells, or so-called new ducts, are met with under such various circumstances that their existence is of no value as an indication of the cause (p. 496). Goodhart doubts the formation of *new* ducts, and thinks the old ones simply become more conspicuous owing to the atrophy of the liver-cells.*

The liver-cells are stated by many to undergo active changes, and to contribute to the formation of the "new ducts," and even of

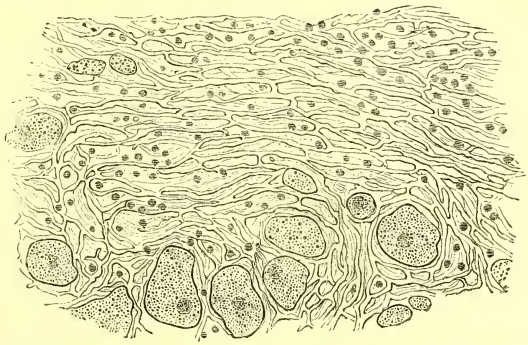


FIG. 179.—*Cirrhosis of the Liver.* A thin section from the external portion of one of the hepatic lobules. Showing the new growth of connective-tissue, and the way in which it involves the intercellular network and causes atrophy of the liver-cells. × 200.

the cicatricial-tissue (Hamilton). They are in most cases infiltrated with fat—**fatty infiltration** being associated with the cirrhosis (Fig. 180).

The general distribution of the new tissue is described by Charcot as—**multilobular**, **unilobular**, and **intercellular**. In the multilobular form, groups of lobules are surrounded; in the unilobular, each lobule; and in the intercellular, the growth invades the intercellular network. These several modes of distribution are frequently associated, all perhaps being found in different parts of the same organ; and although supposed by Charcot to indicate ætiological varieties, the differences are probably to be ascribed rather to differences in the site of the irritant. This may be conveyed mainly in the

* The subject is ably discussed by Dr. Goodhart in his "Résumé of Diseases of the Liver," *New Sydenham Soc. Atlas of Path.*, Fas. iv.

branches of the portal vein, the radicles of the bile-ducts, or the ramifications of the hepatic artery.

The effect of the new growth is ultimately to cause atrophy of the hepatic cells, and to obstruct the circulation through the portal capillaries and the passage of bile through the bile-ducts. The first of these effects is generally more marked than the second. The blood-pressure in the portal vein rises, and after a time ascites follows. The pressure is materially increased by the process of contraction which

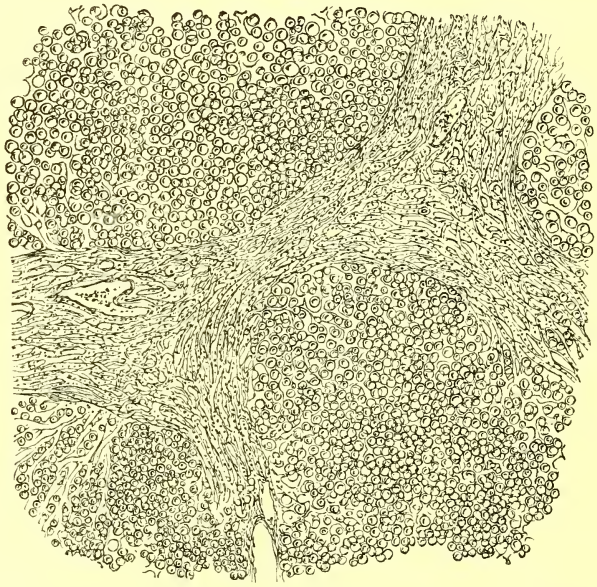


FIG. 180.—*Liver.*—Cirrhosis with fatty infiltration. × 100. Reduced ⅓.

the new tissue undergoes. The hepatic cells in the outer zone of the lobules are the first to atrophy. The cells shrivel, or become distended with fat (Fig. 180), and ultimately are completely destroyed (Fig. 179). Those in the central parts of the lobule are in the earlier stages but little altered, although they are often stained with bile. As the growth extends, however, these also become annihilated, and the whole lobule may be replaced by connective-tissue. The atrophy of the cells may depend partly on the direct pressure of the new tissue, and partly on the indirect effect by which this cuts off their blood-supply.

PHYSICAL CHARACTERS.—The physical characters of the cirrhosed liver vary. In the earlier stages of the disease, the organ is probably always more or less increased in size; the enlargement being almost uniform, and the edge rounded and thickened. This enlargement very often exists up to the end of the disease, but, in many cases, the atrophy of the liver-cells and the contraction of the new tissue lead to considerable diminution in size. The surface of the organ is usually more or less irregular, sometimes "hobnailed;" the extent of the irregularity depending upon the distribution of the new tissue and the amount of atrophy that has taken place. Multilobular distribution, as compared with unilobular, leads to less enlargement of the liver, but to much greater unevenness of the surface. The consistence of the organ is always more or less increased, although in some cases, where the process is very rapid, the increase is so slight as easily to escape observation. Both irregularity of surface and induration are usually most marked along the anterior edge, especially of the left lobe. On section, the new tissue surrounding the lobules, and in many parts completely replacing them, is often visible to the naked eye. This gives to the cut-surface a mottled granular appearance, the lobules themselves contrasting with the new interlobular tissue, and appearing as yellow foci in a pink network. The capsule may be thickened, and the organ is frequently stained with bile.

The great increase in the size of the liver, which exists in some cases, is due in part to the fatty infiltration of the liver-cells (Fig. 180). In those cases, in which the process is rapid, and the new growth consequently very general in its distribution—unilobular and often intercellular—the organ is usually large; death probably supervening before time has been allowed for much atrophy and contraction to take place. Some of the large livers are supposed to be due to "biliary" cirrhosis, to which reference has already been made (p. 493).

ÆTIOLOGY.—*The* cause of cirrhosis of the liver is *alcohol.* With the exception of syphilis, no other cause can be regarded as proven. The question of a biliary cirrhosis must at present remain an open one. Cirrhosis from syphilis has already been described (p. 382). In the congenital form, the process is often so general in its distribution, as closely to resemble some cases of acute alcoholic cirrhosis.

It is important to remember **clinically** that cirrhosis not only obstructs the portal circulation, thus giving rise to ascites, hæmatemesis, diarrhœa, enlargement of the spleen, and hæmorrhoids, but

that, owing to the destruction of the liver-cells, the functions of the organ are so much impaired that marked interference with general nutrition results. Jaundice is usually slight, probably because the bile-ducts are not obstructed at various points in their course, but are pretty uniformly compressed from their origin onwards.

Acute Yellow Atrophy.

This rare disease of the liver is characterised by a rapid diminution in the size of the organ, accompanied by destruction of the hepatic cells, and is often associated with pregnancy. The liver may, in the course of a few days, be reduced to less than half its natural bulk, being especially diminished in thickness. It is soft and flabby in consistence, bloodless, and of a dull yellow or yellowish-red colour. The lobules are indistinguishable. When examined microscopically, most of the liver-cells are found to be completely destroyed, being replaced by granular débris, fat-granules, and pigment. Tyrosin and leucin have been found in the disintegrated liver-tissue. Branched tube-like collections of cubical cells, suggestive of bile-ducts, are frequently seen among the surviving stroma (p. 493). The pathology of this disease is exceedingly obscure. By some it has been regarded as a passive degeneration, by others as an acute infective inflammation. Micrococci have been found in the organ, in early stages of the disease, by Dreschfeld and others.

CHAPTER XXX.

INFLAMMATION OF THE KIDNEY.

Inflammatory processes in the kidney present certain variations according to their intensity. They comprise *suppurative, parenchymatous* and *interstitial* nephritis. Of these, **suppurative** nephritis is an intense inflammation leading to the formation of abscess; and although this form of inflammation is practically limited to the interstitial tissue, the term "interstitial nephritis" is generally reserved for chronic processes. **Parenchymatous** nephritis is an inflammation of considerable intensity, involving glomeruli and tubules. **Interstitial** nephritis is the name applied to a chronic process in which atrophy

probably plays a more important part than inflammation. As in chronic inflammations of other organs, the principal structural changes take place in the connective-tissue around the blood-vessels—*i.e.*, in the intertubular connective-tissue (p. 279). It must, however, be distinctly borne in mind that the histological changes in the tubes and in the intertubular connective-tissue *are very constantly associated.* Parenchymatous and interstitial nephritis cannot therefore be separated from one another by any distinct line of demarcation.

Suppurative Nephritis.

Renal abscesses result from the transmission of infective particles from some primary focus. They may occur as one of the lesions in *pyæmia,* or they may be associated with some *inflammatory condition of the lower urinary passages.* In pyæmia, the infective particles are transmitted by the blood-vessels. In the other cases, they reach the kidney by direct extension from the lower urinary passages. The latter condition forms one of the varieties of the so-called "Surgical Kidney."

The abscesses met with in the kidney, as the result of pyæmia, are confined principally to the cortex, and resemble pyæmic abscesses in other organs. They are usually multiple, and are often surrounded by a thin zone of red hyperæmic tissue. Their size varies from a mere point to that of a filbert. These characters have been already described (p. 446).

SURGICAL KIDNEY.—This is the name commonly given to those inflammatory conditions of the kidney which result from obstructive and inflammatory diseases of the lower urinary passages. They occur in association with renal and vesical calculus, obstructed ureter, urethral stricture, and enlargement of the prostate. These, and similar conditions, may act upon the kidneys in three ways:*—

1. *By obstructing the outflow of urine from the pelvis of the kidney.* Actual regurgitation from the bladder into the ureter is unknown. When the flow of urine from the ureter into the bladder is prevented by any form of obstruction, the full force of secretion, aided by gravity, seems to expend itself in dilating and irritating the ureter, the pelvis,

* The views here expressed are in accordance with the teaching of Marcus Beck. "Nephritis and Pyelitis consecutive to Affections of the Lower Urinary Tract," *Reynolds' System of Medicine,* vol. v.

and the pyramids, and, finally, the tubules even to their closed ends When the obstruction to the outflow is confined to *one* kidney, that organ is alone affected.

2. *By producing reflex changes in the circulation through the kidney.* A close relationship seems to exist between the deeper portions of the urethra, the prostate and the trigone, on the one hand, and the kidneys, on the other. An intense hyperæmia due to irritation of the nerves of these parts, as in some operations, may in extensively diseased organs lead to arrest of the circulation and death from suppression of urine.

3. *By extension of decomposition from the bladder to the kidneys,* and irritation of the latter by septic products. As regurgitation does not occur, decomposition often remains limited to the bladder. When extension occurs, it is probably due to the presence of ropy mucus, lying as a cord in the opening of the ureter, when this has become inflamed from other causes. Such mucus acts as a culture-ground along which organisms can grow.

The morbid changes in the kidney vary from the most chronic productive inflammation, to an acute suppurative process.

Simple long-continued increase of urinary pressure, resulting from some obstruction to the flow of urine, gives rise to chronic renal changes, which are characterised mainly by more or less cellular infiltration of the intertubular connective-tissue, and atrophy of the tubular epithelium (p. 505). This cellular infiltration, which is exceedingly irregular in its distribution, occurs both in the pyramids and cortex. The tubules are in some parts found blocked with epithelium, whilst in others they are wasted or obliterated. The walls of the small arteries are not thickened. Owing to these changes, the kidneys are somewhat enlarged, the capsule is slightly adherent, the cut-surface is paler than natural, and the consistence of the organs is abnormally tough. As the process advances, the pyramidal portions gradually become absorbed, the absorption commencing at the papillæ and extending, until ultimately not only the pyramids but also the thickened cortex may disappear, and the kidney be converted into a large cyst divided into sacculi by fibrous septa. If, on the other hand, the urinary obstruction be removed, the processes of inflammation and absorption may cease, and the indurated kidney will then become contracted.

In other cases, when the urinary obstruction is associated with inflammation of the lower urinary passages, the process is much more

acute, the cellular infiltration of the intertubular tissue is much more abundant, and, in certain situations, leucocytes accumulate in such



FIG. 181.—*Surgical Kidney.* At the lower part of the figure is seen the cellular infiltration of the intertubular tissue, and the blocking of the tubes with epithelium and leucocytes. At the upper part, there is the commencing formation of an abscess. × 100. (Boyd.)

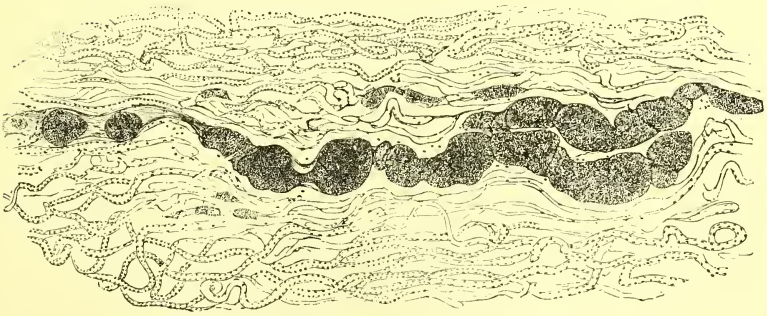


FIG. 182.—*Surgical Kidney.* Showing crowds of micrococci ascending along the tubules. Almost all nuclei in their vicinity have disappeared. They seem to have caused coagulative necrosis of the tissues. × about 90. (Boyd.)

numbers, as to give rise to abscesses (Fig. 181). The cortex of such a kidney is thickened, soft, and pale as compared with the deep red pyramids; its consistence, however, will vary with the presence or

absence of chronic interstitial changes. The capsule strips easily, often tearing the substance a little, and exposing on the surface groups of yellow spots. These yellow dots are never larger than a lentil; each is surrounded by a red zone, and many of them contain a drop of pus. On section, yellow streaks are often seen extending from the superficial lesions into the cortex; others exist in the pyramids. The pelvis is generally intensely inflamed.

Klebs found many of the convoluted tubes crammed with micrococci. These seem to ascend from the pelvis along the tubes, distending them, and setting up irritative and degenerative processes along their line of passage. When stained with an aniline dye, the appearance shown in Fig. 182 is seen. It is extremely probable that these organisms are the cause of the suppuration. The urine in the pelvis of such kidneys is usually, but not always, septic.

Parenchymatous Nephritis.

Parenchymatous nephritis may be *acute* or *chronic*, *primary* or *secondary*.

The **primary** variety comprises the common forms of acute and chronic Bright's disease—forms characterised by a distinct onset, scanty and highly albuminous urine, and dropsy. In its more advanced stages, it is the large white kidney of Bright's disease. These varieties are termed *primary* because their exact causation is unknown.

The **secondary** forms of parenchymatous nephritis occur as complications of infective diseases, especially scarlatina. In pneumonia, and some other diseases, the organism associated with the primary condition has been found in the inflamed kidney; and the nephritis is, in these cases, supposed to be due to the action of the organisms and their products.

The parts in which changes have been observed are: (1) the glomeruli; (2) the convoluted tubes; (3) the small arteries; and (4) the intertubular tissue.

In the most acute cases of **primary** Bright's disease—those which occur suddenly, as after exposure to cold—*vascular dilatation is marked.* In these cases, the contraction of the cutaneous vessels and the check to the function of the skin, caused by the chilling of the surface, lead to considerable hyperæmia of the organs. There is abundant exudation into the tubes; at the same time, many of the capillaries forming

the Malpighian tufts, rupture, so that there is also an escape of blood-corpuscles and of liquor sanguinis into the tubes of the cortex—hence the blood and "blood-casts" in the urine which are so characteristic of the early stages of the most acute forms of the disease. In the kidneys of persons dying at this stage, large numbers of red corpuscles may be seen in the Malpighian bodies pushing to one side the vascular tufts; and in the tubes, which may be consequently distended. At this stage, the process may quickly subside, and, with the exception

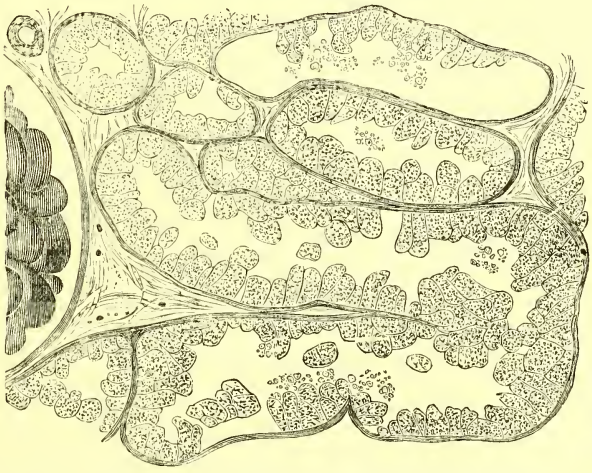


FIG. 183.—*Tubal Nephritis.* The earlier stage of the process. Showing the swelling of the tubular epithelium, and some exudation-products in the urine-tubes. In some of the tubes the epithelium has fallen out during the preparation of the section. × 200.

of some swelling and desquamation of the tubular epithelium, no further alterations take place in the kidney.

In the less acute cases—those known as subacute Bright's disease with large kidney—the vascular phenomena are less marked, and the *changes in the tubular epithelium are more prominent.* The epithelial elements undergo cloudy swelling (p. 63), (Fig. 183). Many small cells are seen partially filling up the tubes. These are supposed to be mainly the products of epithelial proliferation, though some of them are in all probability leucocytes escaped from the vessels (p. 483). Owing to these changes, the tubes become distended with cellular elements (Fig. 184). A varying number of new cells are also found around the Malpighian tufts (p. 504).

In addition to the cell-forms, many of the tubes also contain hyaline cylinders, or **casts**, which are commonly regarded as consisting of coagulated exudation. By many pathologists, however, this hyaline material is supposed to be the product of a mucoid or some allied metamorphosis of the epithelium. The cell-forms contained within the tubes adhere to this hyaline substance, and some of them are washed away and appear in the urine as "epithelial casts."



FIG. 184.—*Tubal Nephritis — a Single Urine Tube.* Showing the accumulation within the tube. In the few epithelial cells which have escaped, the granular condition of the protoplasm is seen. × 200.

The alterations which these changes produce in the *naked-eye characters* of the kidneys vary according to the extent of the hyperæmia. The organs are always considerably increased in size, and more or less abnormally vascular. The capsule separates readily, exposing a perfectly smooth but vascular surface. The consistence is diminished, the tissue breaking with a soft, friable fracture. On section, the increase in the size of the organ is seen to be principally due to the increased thickness of the cortex. This is either of a reddish-brown, or of an opaque-white or pale buff colour: these differences depend upon the relative proportion of blood and of accumulated intratubular elements. Although in the earliest stage of the most acute forms of the disease, the colour is redder than natural, it soon becomes pale and opaque. This is owing to the swelling of the epithelial elements and to the accumulation of cells in the cortical tubes. The blood becomes expressed from the intertubular vessels, and hence the increased vascularity is most evident in the Malpighian corpuscles, beneath the capsule, and in the pyramidal portions of the organ. The Malpighian corpuscles stand out as prominent red points, and the pyramidal cones are of a deep red colour, thus contrasting strongly with the pale opaque cortex.

The *termination* of the process varies. The increased vascularity and epithelial change may, as already stated, subside, and on the inflammatory products passing away in the urine, the organ will gradually return to its normal condition. In other cases, the disease continues; and although the vascularity diminishes, the vitality of the epithelial elements is so much impaired that they undergo retrogressive changes. In these cases the cells still continue to come away with the urine, but instead of presenting a swollen granular appearance, as in the

earlier stage of the disease, they now contain molecular fat. This fat gradually increases in amount as the degeneration proceeds, until ultimately the cells are destroyed, and the fat appears as free molecules and granules on the tube-casts.

This fatty degeneration of the epithelium is attended by corresponding changes in the appearance of the organ. The redness diminishes, and the Malpighian corpuscles are less prominent. The enlarged cortex presents a yellowish-white tinge, studded with minute yellowish streaks. This is owing to the presence of fat in the tubes of the cortex. This fatty stage, if only slightly advanced, may undoubtedly pass off. The degenerated cells are carried away by the urine. From

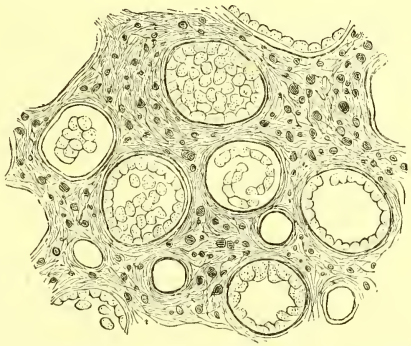


FIG. 185.—*Tubal Nephritis.* Duration of disease, six months. Kidneys, large; capsules, non-adherent; surface, smooth; tissue, soft. Showing, in addition to the intratubular change, the cellular infiltration of the intertubular connective-tissue. × 200.

those which remain in the tubes, the fat is probably partially absorbed. Thus the retrograde process gradually ceases, and the organ returns to nearly its normal size and condition. In other cases, the degeneration continues, and, owing to the loss of epithelium, the kidney becomes somewhat diminished in size. This atrophy is always accompanied by changes in the intertubular connective-tissue.

When the inflammatory process is of *still longer duration,* or when the kidneys are the seats of repeated attacks of subacute inflammation, *the intertubular connective-tissue invariably becomes involved.* This tissue becomes infiltrated with small cells which ultimately tend to form a fibrillated structure (Fig. 185). The new intertubular growth may gradually increase, and so lead to more or less irregular atrophy of the organ, such as will be described as occurring in interstitial nephritis (small white kidney). The new tissue is more uniformly distributed,

and the contraction less marked in those cases following tubal nephritis than in those presently to be described (p. 505). In other cases, death ensues before any marked atrophy has taken place, and thus the organ may remain smooth and large to the termination of the disease (large white kidney). The intertubular growth is sometimes found thickly studded with fatty granules. Attacks of subacute inflammation not infrequently occur in the course of the more chronic cases of primary parenchymatous nephritis.

The **secondary** forms of acute parenchymatous nephritis (*scarlatinal nephritis*) are mainly characterised by changes expressed by the term glomerulo-nephritis.

The *earliest* and most marked changes are often confined to the Malpighian bodies. These are found to contain a number of *new cells*, the exact origin of which is uncertain. According to some, they are derived from the endothelial cells of the vascular tufts; according to others, they are accumulated leucocytes; and in the opinion of others, again, they are the progeny of the epithelium covering the glomerulus. The new cells are sometimes accompanied by so much exudation that the vascular tuft is compressed, and the circulation through it more or less interfered with (p. 501).

The *intima* of the minute arteries, especially of those supplying the glomeruli, is frequently swollen (hyaline degeneration); and an irregular narrowing of the lumen of the affected vessels is thereby produced. This change may be also present in the capillaries of the glomeruli, in consequence of which many of them become impermeable. The *muscular walls* of the minute arteries are also thickened, and the nuclei multiplied. Cloudy swelling of the epithelium in the convoluted tubes is commonly superadded.

Later on, a cellular infiltration of the intertubular connective-tissue of the cortex may occur, together with an increase in the epithelial degeneration, and a crowding of the tubes with small round cells. The cellular infiltration commences around the larger vascular trunks, whence it spreads rapidly into the bases of the pyramids, and especially into the cortex. As it increases, the epithelium undergoes fatty degeneration, and the urine-tubes gradually become obliterated.

To the *naked eye*, in the *acuter* varieties of glomerulo-nephritis, no change is visible. In the *later stages*, when the disease has lasted several weeks, the glomeruli may be unduly prominent, the interpyramidal portions of the organ enlarged, and yellowish streaks visible in the cortex.

Interstitial Nephritis.

We have already seen that an increase in the interstitial tissue of the kidney occurs in the more advanced stages of parenchymatous (p. 503), and of chronic consecutive nephritis (p. 498). But this change is most frequent and prominent in that most chronic of all varieties of Bright's disease which is known as contracted kidney, granular kidney, cirrhosis of the kidney, gouty kidney, or interstitial nephritis. This disease is associated pathologically with atrophy of the glomeruli and tubules, and changes in the walls of the arteries. Clinically, it is characterised by an insidious onset, an increased blood-pressure, a large secretion of urine, and the gradual development of hypertrophy of the left ventricle of the heart. Albuminuria, if present, is slight, and dropsy is absent.

Naked-eye Appearances.—In a well-marked case, the kidney is much diminished in size. Its capsule is thick and very adherent; it

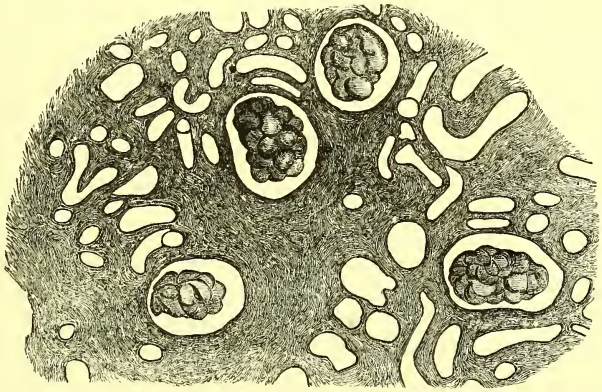


FIG. 186.—*Interstitial Nephritis.* A very advanced stage of the process. Showing the large amount of tissue between the tubes of the cortex, and the extensive atrophy of the tubes. The degenerated epithelium which was contained in some of the tubes has fallen out in the preparation of the section. × 150.

cannot be removed without tearing the substance. The surface is coarsely granular and of a reddish-grey tint. On section, the colour of both pyramids and cortex is seen to closely resemble that of the surface, the distinction between cortex and pyramid being often by no means clear. The cortex is, however, more mottled, and small patches

can sometimes be made out corresponding to the depressions between the minute nodules on the surface. Moreover, it is much narrower and



FIG. 187.—*Interstitial Nephritis.* An advanced stage of the process. Showing the intertubular tissue with the granular and fatty débris which result from the degeneration. × 100.

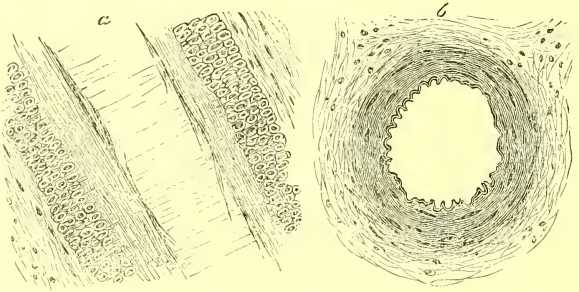


FIG. 188.—*Arteries from Contracted Kidney of advanced Chronic Bright's Disease.* *a.* Longitudinal section, showing the great thickening of the circular muscular coat, also of the outer fibrous coat, and the internal connective-tissue layer. *b.* Transverse section of another vessel less diseased. Here is seen the thickening of the circular muscular and external fibrous coat. × 200.

tougher than normal; and small cysts are often found, especially on its surface. Calcareous deposits may occasionally be seen as white streaks among the tubes of the pyramids. In the earlier stages of the disease, all these changes will be much less marked.

Microscopic Characters. — If one of the depressions just mentioned be examined, it will be found to consist of a number of shrunken Malpighian bodies and a few atrophied or distended tubes embedded in a mass of fibroid tissue (Fig. 186). Bowman's capsule may, in each case, be more or less thickened.

The rest of the cortex is by no means uniformly affected. In many parts, the tubes are diminished in size or completely obliterated: in others, they are dilated and filled with degenerated epithelial products (Fig. 187). Their walls are often thickened. The intertubular tissue is increased throughout, but by no means uniformly. The new tissue may be largely cellular or densely fibroid. The atrophy of the Malpighian bodies and adjoining tubes may be out of proportion to the amount of fibrous overgrowth.

Attention must now be turned to the interlobular arteries and the smaller cortical vessels. The walls of these are almost invariably thickened. Sometimes the external coat is principally involved, and appears to be continuous with the new intertubular tissue. Sometimes the middle coat is thickened, as in the specimen from which the accompanying illustration was taken (Fig. 188). Johnson attributes this to hypertrophy of the circular muscular fibres. Recent observers emphasise the frequency with which the intima is involved: the endarteritis thus produced most closely resembles that form already described as syphilitic (p. 432). The changes in the arteries are by no means limited to those of the kidneys, but are found in the arteries of almost any part of the body.

Pathology.—The relationship these changes bear to one another must now be considered. It is by no means certain that this relationship is, in all cases, the same. Two explanations have been suggested. According to the first and older view, the changes are due to the action of some unknown irritant conveyed by the blood to the kidneys, thus giving rise to proliferation of the connective-tissue in the immediate neighbourhood of the vessels (Fig. 189). According to this explanation, a granular kidney is analogous to a cirrhotic liver. The thickening in the vessels, and the increase in the intertubular tissue, are the earliest, and practically simultaneous, changes; while the atrophy of the secreting tissue is due to the results of the contraction of the chronic inflammatory tissue.

According to the more recent and now more generally accepted view, the order of events is reversed. The secreting-tissues, from overwork, and from the premature exhaustion of their inherited vital capacity, are

unable to utilise such nourishment as is supplied by the blood, which in most, if not all, cases is defective or even deleterious. The secreting tissues, constituting the most highly organised part of the kidney, will have the greatest difficulty in assimilating nourishment under abnormal conditions, and, in any general interference with nutrition, will therefore be those most likely to suffer. Thus, the shrinking of the glomeruli and tubules form the initial change (Fig. 186). The changes in the blood-vessels and the increase in the interstitial tissue follow. The latter is, in many cases, more apparent than real, being partly due to the mere condensation of the previously existing, but more widely

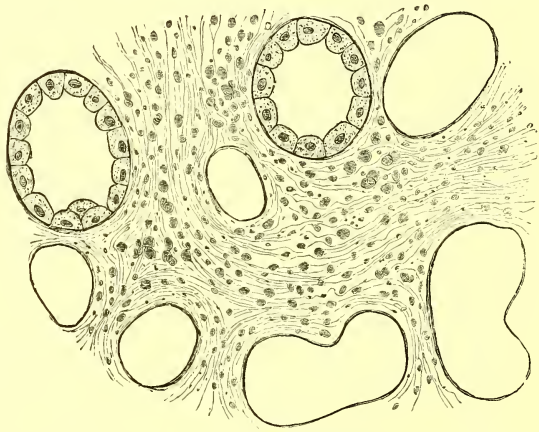


FIG. 189.—*Interstitial Nephritis.* Showing marked increase of the intertubular connective-tissue. The epithelium has fallen out of some of the tubes during the preparation of the section. × 200.

separated tissue. To some extent, it may be the result of irritation, and be partly inflammatory in its origin.

The subsequent contraction of the new tissue necessarily constricts many ducts. The arrest of the flow, in those supplied by glomeruli whose vessels are still permeable, will lead to the formation of small retention-cysts, such as have been previously described.

Sometimes the arterial changes are more marked than the atrophy of the glomeruli and tubules. In these cases, the endarteritis, by diminishing the lumen, and hence the blood-supply, is possibly responsible for the production of the atrophy.

Clinically, *granular kidney* is a disease generally, but not exclusively, limited to the declining period of life It is often associated with

gout, chronic lead-poisoning, and over-indulgence in alcohol; and, perhaps more often than is generally believed, with syphilis. In all the marked cases, it is accompanied by hypertrophy of the left ventricle of the heart, increased arterial tension, and degenerative changes in other tissues. Cohnheim held that the supply of blood to the kidneys varied with the amount in the blood of those substances which the kidneys are normally in the habit of eliminating. Atrophy of part of the excretory apparatus, by throwing more work on the remainder, might not improbably lead to an increase in the percentage of these substances in the blood. Now, the only way in which the elimination of these by the kidneys can be proportionately increased, is by the increased action of the left ventricle and a simultaneous increase in the resistance in the arterioles of other parts. By this means, a larger amount of blood might be supplied to the kidneys, and their excretory functions thereby assisted. This might result from some reflex mechanism.

The enlargement of the left ventricle is a true hypertrophy, though it is often combined with a small amount of chronic myocarditis.

CHAPTER XXXI.

INFLAMMATION OF THE LUNGS.

In the lungs, inflammatory processes comprise the three following principal varieties: (1) **Croupous**, lobar, or acute pneumonia; (2) **catarrhal**, lobular, or broncho-pneumonia; and (3) **interstitial** or chronic pneumonia. Of these, the first occurs as an independent affection, whereas the last two are usually the result of some antecedent bronchial or pulmonary inflammation.

Acute, Croupous, or Lobar Pneumonia.

Acute Pneumonia is an infective disease characterised by inflammation of the parenchyma of the lung, leading to the solidification of a considerable area of that organ. It is usually limited to one lung, and the right is most frequently affected. The inflammation starts in the substance of the lung, from a focus which, in the majority of cases, is in the lower part of the lower lobe. The disease extends by continuity

of tissue from this primary focus, and necessarily, in most cases, in an upward direction; although it may begin at any point and extend in any direction. There is no reason to suppose that the disease spreads by the bronchial tubes. The consolidated area may exactly correspond to the boundaries of a single lobe; though quite as often it fails to reach them, or oversteps them.

The inflammation of the lung is always accompanied by inflammation of the pleura over the inflamed area, and sometimes, owing to the spread of the infection, by that of the peritoneum and pericardium. The bronchial glands are inflamed and swollen; the mediastinal connective-tissueis frequently œdematous; and acute secondary meningitis occasionally supervenes. The disease is accompanied by high fever, beginning usually with a sudden rise and marked symptoms (p. 254), and ending by crisis: cloudy swelling of organs results. Death, when it occurs, seems to be due to cardiac failure, induced by general poisoning.

ÆTIOLOGY.—This disease was formerly attributed to a chill, and in certain cases, the origin of the disease in connection with exposure to cold and damp is very striking. It is, however, impossible to regard cold as more than a predisposing cause; for exposure to cold is alleged as a cause in only a small minority of the cases. Moreover, the disease does not especially affect those who are most exposed to vicissitudes of weather, nor does its prevalence rise and fall with that of bronchitis. Finally, pneumonia cannot be produced by exposure to cold, or by the infliction upon the lung of any mechanical or chemical injury. Similarly, depressed health is only a predisposing cause. Typically healthy people are often affected.

In the present state of our knowledge, we should naturally expect to find that some organism is the cause of such a disease as pneumonia; especially when we know that, though there is not the least evidence of contagiousness, yet in some years it is so prevalent as to be practically epidemic. Again, small outbreaks occasionally occur in wards, prisons, and similar places; and the disease is sometimes endemic in a house, from time to time attacking different people in it. In the large majority of cases, the disease is *probably* due to the growth of the diplococcus pneumoniæ (p. 355). It is not certain that all cases of primary acute pneumonia are due to one and the same parasite; and it is still more doubtful whether secondary acute pneumonia, arising in the course of such diseases as typhoid or erysipelas, always owes its origin to the same organism.

By most pathologists the disease is regarded as an infective inflammation of the lung, just as erysipelas is of the skin—the fever being secondary to the inflammation, and due to the passage into the blood of pyrogenic ferments. Others believe it to be a general infective disease, like scarlatina—the lung-inflammation being the characteristic local lesion, corresponding to the rash and throat of scarlatina. The "typical" course of the fever, ending usually in a crisis between the fifth and eighth days, and the absence of any constant relationship between the extent of the local inflammation and the intensity of the fever, are generally regarded as being in favour of the latter view. The results of inoculation-experiments support the former. The essential difference between the two views would seem to be that the blood is infected from the lung according to the first, whilst, in the second, the irritant reaches the lung from the blood, having entered perhaps through the alimentary mucosa.

Pneumonia is prone to recur in a person who has once suffered from it.

MORBID ANATOMY.—The local process is characterised by intense inflammatory hyperæmia of the lung, and by the exudation of a large amount of coagulable material into the pulmonary tissue. It is termed "croupous" from the fibrinous character of the exudation. The term "lobar" is applied to it because it almost invariably affects an extensive portion of the lung. The process is commonly described as consisting of three stages—(1) that of *engorgement;* (2), that of *red hepatisation;* and (3) that of *grey hepatisation.*

In the *first* stage, that of **engorgement**, the lung becomes exceedingly vascular, the changes in the blood-vessels and circulation being those already described as characteristic of inflammation (p. 262). The organ is of a dark-red colour, its specific gravity and absolute weight are increased, its elasticity is diminished, its substance is less crepitant and more friable than natural, and its surface pits upon pressure. On section, it yields a reddish, frothy, tenacious liquid.

In the *second* stage, that of **red hepatisation**, there is an exudation of liquor sanguinis and migration of blood-corpuscles into the pulmonary tissue. Some of the vessels may also rupture, and thus small extravasations occur. The exuded liquids coagulate within the air-vesicles and terminal bronchioles, to form a semi-transparent coagulum enclosing red corpuscles and leucocytes in its meshes (Fig. 190). The fibrin-filaments, according to Weichselbaum, are much thicker

and more numerous in cases due to the diplococcus pneumoniæ. Contrary to the usual rule in acute inflammations, the mononucleated leucocytes are as plentiful as the multinucleated. The pneumococci may be found in both. The lung is now much heavier than in the preceding stage, and is increased in size, so as to be often marked by

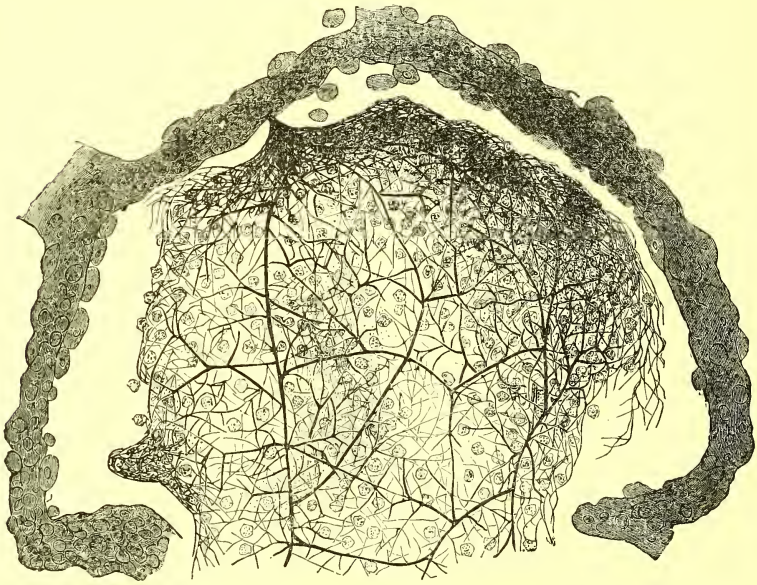


FIG. 190.—*Croupous Pneumonia—Red Hepatisation.* Showing the fibrinous coagulum in one of the pulmonary alveoli, enclosing within its meshes numerous leucocytes, which are already commencing to undergo fatty metamorphosis. A few leucocytes are seen on the alveolar walls, and the alveolar epithelium is swollen and granular. The separation of the coagulum from the alveolar wall is due to the method of preparation. × 200.

the ribs. The affected portion can be recognised before a section is made, for the pleura over it is hyperæmic, opaque, and covered with lymph ; while the distension, firmness, and dark purple colour of the lung beneath cannot escape notice. It is quite solid, sinks in water, and cannot be artificially inflated. It does not crepitate under the fingers, and is remarkably friable, breaking down readily with a soft granular fracture. The cut-surface has a markedly granular appearance, seen especially when the tissue is torn. This is owing to the plugs of coagulated exudation, which project from the alveoli they fill.

There is no lobulation of the margin of the inflamed area, no outlying racemose nodules or other indication of infection spreading by the bronchi. The colour is of a dark reddish-brown, often here and there passing into grey. This admixture with grey sometimes gives a marbled appearance. The red colour is due chiefly to vascular engorgement, but partly to extravasated red corpuscles. Throughout this stage, there appears to be but little alteration either in the

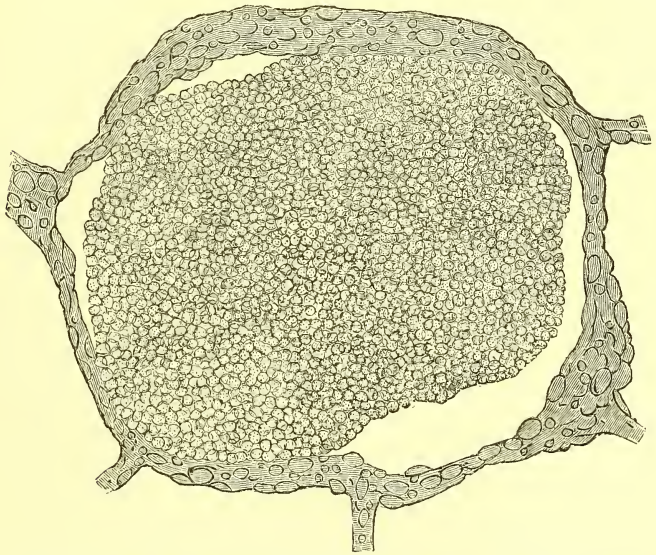


FIG. 191.—*Croupous Pneumonia—Grey Hepatisation.* Showing the large accumulation of cellular elements within one of the pulmonary alveoli, which in some parts have undergone such extensive fatty degeneration that their distinctive outlines are no longer visible. × 200.

alveolar walls or in the alveolar epithelium. In the former, are often seen a few leucocytes, while the latter is usually swollen and granular (Fig. 190). If a section of the spreading edge be examined at this stage, it will be found intensely hyperæmic. The hyperæmia extends somewhat irregularly into the adjacent tissue, which is otherwise of normal appearance.

The *third* stage, that of **grey hepatisation**, is characterised by a continuance in the emigration of leucocytes, and by more marked changes in the epithelium. The white blood-corpuscles continue

to escape from the vessels, until they seem to fill the alveoli. The epithelial cells lining the alveolar walls become more swollen and granular, and the walls themselves become more or less infiltrated with leucocytes. The walls and the contents of the alveoli now assume a uniform appearance, and the granular appearance of the red stage is lost (Fig. 190). The fibrinous material next disintegrates, and the white cells rapidly undergo fatty changes, whilst the red are decolorised; so that the alveoli are seen to be full of granular elements, which in many parts have lost their distinctive outlines (Fig. 191). Occasionally, when this stage is unusually advanced, the alveolar walls may be found, here and there, partially destroyed. The weight, density, and friability of the lung now become even greater than in the stage of red hepatisation, although the granular aspect of the cut-surface is much less marked. The tissue is soft and pulpy, and a puriform liquid exudes from its cut-surface. The most prominent feature, however, is the alteration which takes place in the colour of the organ. This gradually changes from a dark reddish-brown to a grey or yellowish-white, marbled by the tracts of pigment-bearing connective-tissue. The pallor is owing partly to the fatty degeneration which the cells have undergone, and partly to the pressure exercised upon the blood-vessels by the exuded substances and newly-formed cells; but since Rindfleisch has shown that it is always easy to inject the vessels, it would seem likely that a good deal of the pallor is due to post-mortem expression of blood. The stage of grey hepatisation, when far advanced, has been termed "suppuration, or purulent infiltration, of the lung." This stage, in all probability, only occurs in fatal cases.

Although these three stages of the pneumonic process have been described as succeeding one another in orderly succession, it must be remembered that each stage does not occur simultaneously throughout the whole of the affected area of the lung. The changes advance irregularly, so that whilst one portion of the lung is in the stage of red hepatisation, another may be in the grey stage—hence the mottled, marbled appearance of the consolidation. The rapidity also with which the several stages succeed one another is subject to marked variations. In some cases, the pneumonic consolidation very rapidly becomes grey, whilst in others, the time occupied in the transition is several days longer.

The bronchi of the affected area are always inflamed and usually contain a viscid, blood-stained, rust-coloured mucus, which forms the

characteristic expectoration. Sometimes the sputum is dark and watery, like prune-juice. This is probably owing to the addition of œdema-fluid from neighbouring parts of the lung.

TERMINATIONS.—The pneumonic process may end in one of four ways.

1. **In Resolution.**—The gradual return of the lung to its normal condition is the natural and much the most frequent termination of croupous pneumonia. This is effected by the fatty and mucoid degeneration of the inflammatory products which have accumulated within the alveoli. Thus altered, they can be removed by absorption. This process is assisted by the return of the blood-vessels to a normal condition and the re-establishment of the circulation. Granular pigment, derived from the escaped red corpuscles, is often mixed with the softened matters, and appears in the expectoration. It is usually taught that, where this process of resolution is taking place in the lung, the granular appearance of its cut-surface is completely lost; that it is of a yellowish-grey colour; and that a tenacious puriform liquid can be expressed from its substance. But, obviously, we do not know the appearances of cases which recover. The sputum gives no support to the view that resolution takes place by the cell-infiltration and general softening of grey hepatisation; and it seems probable that those pathologists are right who hold that from the stage of advanced grey hepatisation no lung ever recovers.

2. **In Abscess.**—The formation of abscess is a rare result of pneumonia. Such a result appears to be favoured by a bad constitution, and by any circumstances which tend to impair the general health, especially the abuse of alcohol. The abscess is more common in the upper than in the lower lobes. Circumscribed gangrene of the lung also may occasionally terminate in abscess. This takes place by the expulsion of the necrosed tissue through the bronchi, and the formation of a layer of granulation-tissue upon the walls of the cavity, which generates pus. The cavity may ultimately close by granulation and cicatrisation. These abscesses of primary origin are usually single, and thus differ from those due to pyæmia.

3. **In Gangrene.**—This result is also rare, and is also chiefly found in drunkards and in persons of debilitated constitution. Two conditions appear to be principally concerned in bringing about this result:—(1) the interference with the supply of blood by extensive formation of coagula in the pulmonary and bronchial vessels, together

with considerable hæmorrhage into the pulmonary tissue; and (2) the injurious influence of septic inflammatory products. The gangrene is usually limited to a small area of the pneumonic lung, and is either diffuse or circumscribed.

4. **In Chronic Pneumonia**.—If the inflammatory process does not subside, and the exuded substances are not absorbed, the alveolar walls gradually become involved. These become thickened by a new growth of fibro-nucleated tissue, and thus is produced more or less fibroid induration or cirrhosis of the organ. This termination of croupous pneumonia is comparatively rare (p. 521).

Lobular, Catarrhal, or Broncho-Pneumonia.

Broncho-pneumonia is an inflammation of the parenchyma of the lung, due to an irritant entering and spreading by the bronchi. This irritant generally gives rise to a catarrh of the smaller bronchi, to which the pneumonia is secondary.

ÆTIOLOGY.—*Simple*, or *non-specific broncho-pneumonia* signifies the extension of *simple bronchitis* to the alveoli. It is very apt to occur in young children and in aged persons, and often, in such cases, ends fatally. This result, however, must not be attributed to the mere supervention of a few small patches of inflammatory consolidation in the lungs, though this, doubtless, raises the temperature and increases the dyspnœa. It is due rather to the preceding extension of the bronchitis to the finer tubes, for death is due to exhaustion and asphyxia.

The exciting cause of *simple* bronchitis is unknown, although cold is such a strong predisponent that it often *seems* an excitant. There are many irritants which, gaining access to the air-passages, can excite bronchitis and, less frequently, broncho-pneumonia as well. Among them may be mentioned—*irritant-gases; dust* of various kinds, such as particles of carbon (p. 92), steel, iron, or stone, all of which differ much in their irritant power; and *organisms*, of which by far the most important is the bacillus of tubercle—for tubercular broncho-pneumonia is *the* lesion of phthisis; among other organisms which may enter the lungs by aspiration, are the actinomyces and the bacillus of glanders, and apparently also the specific causes of the bronchitis of measles and pertussis.

Lastly, portions of *food* or *saliva, carrying septic germs*, may enter the

air-passages, especially when the glottis is insensitive. During operations on the mouth or nose, or as a consequence of wounds or diseases of these parts, *blood* and *putrid discharges* may also be sucked into the bronchi. Any of these may give rise to suppurative or gangrenous broncho-pneumonia. Simple bronchitis, and those specific forms due to measles, whooping cough, variola, diphtheria, and tubercle are by far the commonest varieties of broncho-pneumonia. Tubercular broncho-pneumonia frequently affords an instance of the occurrence of this form of pneumonia without any appreciable bronchitis, though signs of bronchitis at the apices are often some of the earliest indications of tubercle. Tubercular broncho-pneumonia also affords frequent exceptions to the rule that, being consecutive to bronchitis, both lungs will be affected.

All conditions depressing the general health and strength predispose to broncho-pneumonia. They do this by weakening the resistance of the tissues, and thus permitting the primary infection, as well as the subsequent spread of the inflammation. Possibly, they may also act by diminishing the power of the respiratory muscles, and thus favouring the occurrence of pulmonary collapse, as the finer tubes become blocked by the swelling of the mucous membrane and the presence of the catarrhal secretion. Collapse often seems to precede the inflammation; but evidence of its importance as a predisponent to broncho-pneumonia is unsatisfactory: it may, by interfering with the circulation in the collapsed alveoli, still further weaken the resistance of the tissues, and thus render infection easier. But whenever bronchitis has reached the finest tubes, extension of the inflammation to the alveoli seems natural without assistance from collapse, such extension being probably assisted by the act of inspiration, which would tend to draw the contents of the bronchioles into the alveoli.

PATHOLOGY.—Broncho-pneumonia has been studied experimentally. Animals have been made to inhale irritant gases or suspended particles of various kinds. Further, by division of the vagus, saliva and food have been permitted to enter the air-passages. The resulting changes vary (1) with the *size* of the inhaled particles, and (2) with the *intensity of the irritation* they are capable of exciting. Thus, very fine particles cause widely scattered miliary foci of inflammation; larger ones block the smaller bronchi, and cause collapse and secondary inflammation of lobules—a result which has led to the name of "lobular pneumonia." The aspiration of a quantity of septic dis-

charge or other fluid into a bronchus may affect many lobules or even a whole lobe. According to the intensity of the inhaled irritant, the result may vary from mere collapse, accompanied by slight inflammatory œdema, through all stages of inflammation up to gangrene. In the tubercular form (p. 528), the inflammatory products caseate.

MORBID ANATOMY.—From the above considerations, it will be readily understood that the post-mortem appearances of the lungs present many variations. The *bronchi* are always more or less inflamed, and contain thick mucus. Ordinarily, the lung-tissue contains a varying number of solid patches. These are due either to collapse or to inflammatory consolidation. Emphysema, with more or less congestion and œdema, is commonly found in their neighbourhood. Patches of *collapse* are particularly common in the lower lobe, especially along its thin border. Sometimes a large portion of a lobe is thus involved; at other times only a few, small, isolated patches. The surface of the **collapsed part** is depressed below the general surface of the lung. It has a dark bluish colour, and is easily inflated from the bronchi. On section, it is dark-red, smooth, and shiny. It is tough, and non-crepitant. Portions of it sink in water. On closer inspection the patches are seen to be more or less conical, with their bases towards the surface of the lung and their apices towards the bronchi with which they are in connection. The pleura over a patch of collapsed lung is normal. A **pneumonic patch** is of conical form, and is airless like the collapsed part: moreover, it is similarly distributed. But its base is raised above, never depressed below, the surface, while it forms a less pliable and more nodular mass. Occasionally when it is of considerable size, its pleural covering may be opaque with inflammatory exudation. On section, the pneumonic patches may be distinct or ill-defined; they usually range in size from a small pea to a hazel-nut. The surface of the section tends to rise slightly above the surrounding tissue: its substance is soft, friable, opaque-looking, smooth or faintly granular, at first dark-red in colour, then passing through greyish-red to greyish-yellow—the lighter colour being central. A turbid red or greyish juice can be pressed from it. Neighbouring lobular patches often blend, and as the diffuse consolidation thus formed becomes paler, firmer and drier, it not infrequently resembles in appearance ordinary grey hepatisation. Sometimes the pneumonic process is found involving patches of collapse. These consequently become swollen, opaque, and œdematous.

When broncho-pneumonia is so extensive that the consolidation is practically "lobar," it is difficult to distinguish it from acute



FIG. 192.—*Broncho-Pneumonia.*—From a child aged four, with capillary bronchitis. A section of one of the patches of consolidation. Showing the stuffing of the alveoli with what appears in the main to be inhaled bronchial secretion. × 200.

pneumonia. Evidence of the blending of lobular masses, and especially the presence of outlying nodules in the neighbourhood of

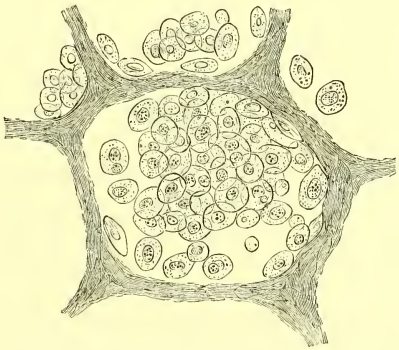


FIG. 193.—*Catarrhal Pneumonia.* From a case of acute phthisis. Showing the large epithelial cells which fill the alveoli. × 200.

the main mass, are the most important points to look for. Absence of inflammatory lymph from the pleural surface is evidence against acute pneumonia; but it must be remembered that such lymph *may* form over a broncho-pneumonic area.

In cases of *septic* broncho-pneumonia—the commonest cause of death after operations on the jaws, mouth, and pharynx—instead of the above solid patches, abscesses occur. These often contain sloughs of lung-tissue and are sometimes fœtid: such sloughs are surrounded by more or less extensive consolidation; and inflammatory hyperæmia and œdema of the lung are marked.

Microscopically, in the early red stage, the alveoli contain fluid, red corpuscles, and a few leucocytes, while the alveolar epithelium is swollen and granular: this latter change, according to Friedländer, is due merely to imbibition, and does not indicate any activity on the part of the epithelial cells. Next, the alveoli become filled with a cell-mass, consisting of leucocytes and cast-off epithelium in varying proportions—leucocytes being in excess in the more acute (Fig. 192), and epithelial cells in the more chronic forms (Fig. 193). In the most acute cases (septic broncho-pneumonia), either suppuration and sloughing occur, or hæmorrhagic exudation with subsequent gangrene.

TERMINATIONS.—Resolution is the most common termination. The contents of the alveoli undergo fatty metamorphosis, and are removed by expectoration and absorption, the lung gradually regaining its normal character. This process, however, is less readily affected than in croupous pneumonia, and it often occupies such a lengthened period that some thickening of the bronchial and alveolar walls, with dilatation of the smaller bronchi, remains. In chronic cases this **fibroid thickening** is much more marked; and considerable, irregularly distributed, pigmented induration and bronchial dilatation may be produced (p. 523). In these chronic forms, **caseation** sometimes affects the contents of the alveoli, which then become encapsuled, or, in quite exceptional cases, disintegrated; but, unless the contrary is demonstrated, all such cases may reasonably be regarded as tubercular.

Hypostatic Pneumonia.—Allusion must be made to a form of lung-consolidation which is often described as pneumonic, but which, in reality, is for the most part not inflammatory in its nature. This is the so-called hypostatic pneumonia. This condition is met with at the bases and most dependent portions of the lungs in the course of both chronic and acute diseases, and also in the aged and debilitated. It consists in the main of collapse, mechanical hyperæmia, and œdema of the lung-tissue, resulting from weak inspiratory power

feeble circulation, and gravitation. The consolidation thus mechanically induced is increased by more or less exudation of liquor sanguinis and blood-corpuscles into the alveoli. This exudation is due to the damage of the walls of the capillaries, caused by the imperfect circulation.

Interstitial or Chronic Pneumonia.

Interstitial or chronic pneumonia is characterised by a gradual increase in the connective-tissue of the lung, which leads to an induration of the pulmonary texture, and to progressive obliteration of the alveolar cavities. It is commonly associated with catarrh and dilatation of the bronchi, and often with ulceration of the bronchial walls and excavation of the indurated lung.

ÆTIOLOGY.—It is very doubtful if interstitial pneumonia is ever a primary and independent affection. In the large majority of cases, it is secondary to some inflammation of bronchi, alveoli or pleura: it results also from persistent atelectasis or collapse. It may be stated generally that all inflammatory processes in the lungs, when they become chronic, lead to an increase of the connective-tissue, and, consequently, to fibroid induration of the organs.

Syphilis certainly gives rise to a gummatous and probably also to a diffuse interstitial pneumonia in children suffering from the congenital form of the disease: of the latter variety, very little is known. In adults, syphilitic changes in the lung are rare: it is very difficult to be absolutely certain of the nature of some localised fibroid changes.

"Brown Induration" (p. 218) has been already described, and will not be further discussed. The chief causes of interstitial pneumonia are:—

1. **Croupous Pneumonia.**—The consolidation of acute croupous pneumonia usually undergoes complete and rapid resolution; but occasionally this is more protracted. Then the hepatised lung tends to become slightly indurated, mainly owing to thickening of the walls of the alveoli. This indurated hepatisation differs but little in its physical characters from ordinary red and grey hepatisation: it is simply somewhat firmer, more resistant, and less granular. In very exceptional cases, this small amount of induration, commencing in the alveolar walls, may gradually increase, so as ultimately to give rise to that extensive fibrosis of the lung which constitutes what is usually known as interstitial pneumonia.

2. **Broncho-pneumonia.**—Broncho-pneumonia is a somewhat more frequent cause than the preceding. The greater liability of this form of pneumonia to lead to pulmonary induration is to be accounted for, partly by its longer duration and greater tendency to become chronic, and partly by the existence of bronchial dilatation, with which it is so frequently associated. The existence of this dilatation favours the persistence of the catarrhal and pneumonic process. The removal of secretion is rendered difficult; and the retained secretion tends to keep up and increase the irritative process both in the dilated bronchi and the pulmonary alveoli, and this persistence of the bronchial and pulmonary inflammation leads to fibroid thickening of the bronchial and alveolar walls. In this way, areas of fibroid induration are produced, which, as the process extends, may ultimately involve large portions of the lung. The progressive tendency of the process is, probably, partly to be explained by the fact that pulmonary fibrosis is itself a cause of bronchial dilatation; when, therefore, fibrosis is once established, the new tissue in contracting induces further dilatation of the bronchi; and this again, as before explained, favours the still further extension of the bronchial and pulmonary induration.

Under this head may also be included those cases of induration and ulceration of the lung which result from obstruction of a main bronchus —such as is produced by the pressure of an aneurysm. Here the retained bronchial secretion sets up inflammatory changes in the bronchial and alveolar walls, which gradually lead to induration and ulceration of the lung.

3. **The Inhalation of Solid Irritating Particles.**—This source of irritation is the cause of the fibrosis of the lung so common amongst miners, potters, stonemasons, grinders, and others. The continuous irritation of the inhaled particles induces a bronchial and alveolar inflammation, and ultimately a progressive fibrosis, with dilatation and ulceration of the bronchi. Such cases often become tuberculous.

4. **Pleurisy.**—This, in exceptional cases, leads to the development of an interstitial pneumonia. Such a result is most likely to occur in those cases of pleurisy which are more or less chronic, and in which the effusion remains long unabsorbed. The induration thus induced is often partial, consisting merely in an increase of the interlobular connective-tissue, originating and extending inwards as dense bands from the thickened visceral pleura. In other cases, pleurisy gives rise to a much more general fibrosis.

5. **Atelectasis**, or failure of part of the lung to expand after birth,

and **persistent collapse** lead to marked cirrhosis of the affected area. Later on, bronchiectasis and obliteration of most of the alveoli occur. The original positions of the latter may be merely indicated by a few epithelial cells.

MORBID ANATOMY.—The appearances presented by the lung, when the fibrosis is general and well advanced, are very characteristic. The organ is diminished in size; the tissue is smooth, dense, firm—in parts almost cartilaginous in consistence; and it is



FIG. 194.—*Interstitial Pneumonia.* From a case of unilateral "cirrhosis" of the lung. The bronchi were much dilated, and there was a complete absence of any caseous change. The drawing shows the new fibro-nucleated growth, both in the alveolar walls and in the interlobular tissue, also the pigmentation. At *a* a divided vessel is seen. With a higher power, a delicate reticulum is visible between the cell-elements. × 100.

irregularly mottled with black pigment. The alveolar structure of the lung is in most parts completely destroyed, and on section, the dilated bronchi are seen as numerous large openings scattered over its surface. These dilated bronchi frequently become the seats of secondary inflammatory processes, which may lead to ulceration and ultimately to extensive excavation of the indurated tissue; but there is a complete absence of any of those caseous changes which are so characteristic of phthisis. This secondary inflammation of the dilated bronchi is induced by the irritating and often putrid secretion which they contain, and which is, as a rule, incompletely removed by expectoration. The pleura is considerably thickened and generally adherent.

Microscopically, a distinct fibro-nucleated tissue is found in the

interalveolar, peribronchial, and interlobular connective-tissue. This new growth, as it increases and contracts, gradually replaces and obliterates the alveolar structure. The character of these changes, however, varies somewhat according to the nature of the inflammatory antecedents in which they originate. When the result of a *croupous pneumonia,* the primary, and usually the principal, change takes place in the walls of the alveoli (Fig. 194), although ultimately the interlobular tissue is involved. The alveolar walls become thickened by the growth of a small-celled tissue, which presents all the appearances found in embryonic tissue which is undergoing fibroid

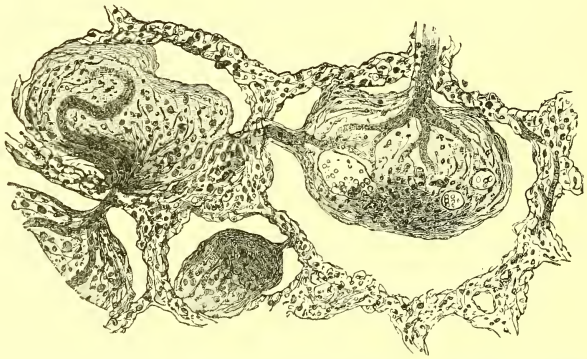


FIG. 195.—*Chronic Pneumonia.* Vascularisation and fibroid development of intraalveolar exudation-products. Blood-vessels are seen distributed in the exudation-products: these blood-vessels communicate with those in the alveolar walls. The alveolar walls are also thickened by a fibro-nucleated growth. × 100, and reduced ½.

development. The new growth, in its earlier stages, contains new blood-vessels, but later on the tissue contracts, and many of these are destroyed. The alveolar cavities which are not obliterated, are either empty, or contain exudation-products or a few epithelial cells. In addition to the growth in the alveolar walls, the author has met with three cases in which intra-alveolar exudation-products were undergoing fibroid development.* There was nothing peculiar in the macroscopic characters of the lungs, but the alveoli were found filled with a fibrinous meshwork and leucocytes, somewhat similar to that met with in red hepatisation (Fig. 195). They differed, however, in this

* For one of these specimens the author is indebted to Dr. Goodhart, who records the case in the *Trans. Path. Soc. Lond.*, vol. xxv. p. 33.

respect—that many of the cells were long and spindle-shaped, and blood-vessels were distributed amongst them, these blood-vessels communicating with those in the alveolar walls (Figs. 195 and 196). The alveolar walls also were thickened by a fibro-nucleated growth. It was therefore perfectly obvious that in these lungs the products of a previous acute croupous pneumonia were becoming vascularised and undergoing development into a fibroid structure, and that this intra-alveolar change was the principal cause of the fibroid induration of the organs.

When the fibrosis is secondary to an ordinary *broncho-pneumonia,* or to that induced by the *inhalation of irritating* solid *particles,* the new

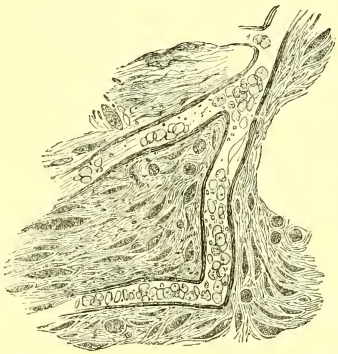


FIG. 196.—*Chronic Pneumonia.* A portion of the intraalveolar exudation-products (Fig. 195) more highly magnified. Showing the elongated spindle-cells, the fibrillation, and blood-vessels containing blood-corpuscles. × 200.

growth also originates principally from the alveolar walls. Here, however, the growth in the earlier stages is less uniform, and the peribronchial and interlobular connective-tissue play a more prominent part in the process (Fig. 197).

The pleurogenic form results chiefly from empyemata. Here the new fibrous tissue extends inwards in bands along the interlobular lymphatic vessels which communicate freely with those of the thickened pleura ; thence it spreads to the peribronchial tissue. The lung is thus surrounded by a dense capsule, and a meshwork of anastomosing fibrous bands permeates its substance, compresses the alveoli, and deforms the bronchi. More or less bronchitis is usually present.

Atelectasis and collapse are said to lead first to slight hæmorrhages.

The subsequent changes in the hæmoglobin lead to the formation (p. 88) of some of the black pigment usually found in fibroid areas



FIG. 197. — *Chronic Bronchitis.* Showing the new growth of fibro-nucleated tissue around the bronchus *b*, and the way in which this tissue is invading the walls of the adjacent alveoli. *v.* A divided blood-vessel. × 100. Reduced ½.

owning this origin. The alveolar walls become fibroid, the epithelium is more or less shed, and the surfaces of the walls ultimately cohere.

PULMONARY PHTHISIS.

By **Pulmonary Phthisis** is understood a disease of the lungs, which is characterised by progressive consolidation of the pulmonary texture, and by subsequent softening and disintegration of much of the consolidated tissue. The upper portions of the organs are, in almost all cases, the first to become involved.

Respecting the nature of the morbid processes which lead to this consolidation and disintegration—various opinions have from time to time been held by pathologists. According to the older views, which were based upon the teaching of Laennec, phthisis was regarded in all cases as a **tuberculous** disease. Tubercle was looked upon as a non-inflammatory growth which was characterised by the caseous degeneration which it invariably underwent; and this caseous metamorphosis was held to be such a distinguishing peculiarity of the growth, that all caseous masses came to be regarded as tuberculous, and phthisis, in which caseation plays such a prominent part, was

consequently regarded as a tuberculous disease. The various consolidations of the pulmonary tissue in phthisis were described as "infiltrated tubercle," and tubercle in some form or other was regarded as so essential a constituent of the disease, that "phthisis" and "pulmonary tuberculosis" came to be synonymous terms. When the application of the term *tubercle* became limited by Virchow and his followers to the *grey granulation*, it was evident that these views were no longer tenable, and many, in accordance with the advocacy of Niemeyer, regarded phthisis as a form of progressive caseous pneumonia, which was quite independent of tubercle, although tubercle might occur as a secondary and accidental complication. It was then said that some cases of phthisis were tubercular, and that others were not; and attempts were made to subdivide the disease into distinct pathological varieties, according to their anatomical and histological characters. In this way, *tuberculous*, *pneumonic*, and *fibroid* phthisis were distinguished from one another. Our present knowledge of tuberculosis, and especially of its ætiology, necessarily involves considerable modification of these views. Before considering the pathology, however, it will be well to study the histology of the disease.

HISTOLOGY.—The histological changes in the lungs which occur in pulmonary phthisis are similar to those met with in these organs in acute miliary tuberculosis. They differ mainly in this respect—that whilst in miliary tuberculosis these changes are limited to small areas (being due to the distribution of bacilli by the blood, and to their deposit here and there in the pulmonary tissue), in phthisis they ultimately *involve* much *wider tracts* of tissue. Further, phthisical consolidation is *lobulated* in its distribution, owing to the fact that the irritant causing the inflammation generally gains access, and is often redistributed through the medium of the bronchi. This lobulated distribution of the consolidation is exceedingly characteristic; and even in those acute cases, in which, owing to the rapid and extensive implication of the lung, the consolidation may, to the naked eye, appear almost as uniform as that in croupous pneumonia, the microscope will usually reveal a lobular distribution (Fig. 198).

The structural changes met with in the lungs in phthisis are mainly of four kinds: (1) an accumulation of epithelial cells within the pulmonary alveoli; (2) the presence within the alveoli of a fibrinous exudation and leucocytes; (3) a cellular infiltration and thickening of the alveolar walls, together with, in most cases, a similar change in

the walls of the terminal bronchioles; and (4) an increase in the interlobular connective-tissue. These four kinds of morbid change are very constantly associated, although in very different degrees; and some of them are more prominent and characteristic than others. The preponderance of one or other of them produces those variations in the physical characters of the lungs which are met with in the different stages, and in the different varieties, of the disease. These various structural changes must now be considered separately, together

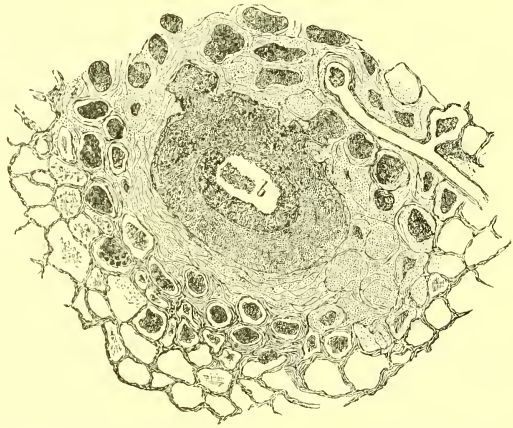


FIG. 198.—*Acute Phthisis.* A transverse section of a terminal bronchus (air-passage) and the surrounding alveoli. Showing the *lobulated* character of the pulmonary consolidation. *b*. Cavity of bronchus containing a little mucus. × 50. Reduced ½.

with the more important alterations which they produce in the physical characters of the organs.

1. **An accumulation of epithelial cells within the pulmonary alveoli.**—This is one of the most frequent changes met with in phthisis, and is precisely similar to that which has been already described as occurring in catarrhal pneumonia (Fig. 193, p. 519). The alveoli are found filled with large nucleated elements, apparently the offspring of the epithelial cells normally lining the alveolar walls (Fig. 199). In some acute cases of phthisis, this alveolar accumulation may constitute almost the only morbid change, and although there is always some cell-infiltration of the alveolar walls, the great bulk of the pulmonary consolidation is due to the stuffing of the alveolar cavities with catarrhal products (Fig. 200). In some

parts—those in which the change is the most recent—the large cells which fill the alveoli and the alveolar walls will be found but little

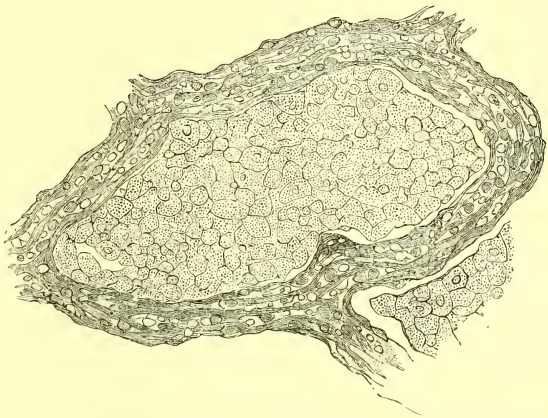


FIG. 199.—*Acute Phthisis.*—Showing one of the alveoli filled with epithelial elements, and marked cell-infiltration of the alveolar wall. × 200.



FIG. 200.—*Section of Lung from a Case of Acute Phthisis.* Showing that the consolidation consists almost exclusively of products accumulated within the alveoli. In some parts a free space is seen between the alveolar walls and their contents; this is due simply to the shrinking of the latter caused by the hardening of the specimen. × 50.

altered; but in the greater portion of the consolidated tissue, the cells will be seen in various stages of retrogressive metamorphosis,

and the alveolar walls destroyed; whilst in those tracts of tissue in which the process is most advanced, all trace of structure is lost, and nothing is seen but a granular débris. These changes are precisely analogous to those met with in many of the larger nodular lesions of acute tuberculosis (Figs. 142 and 143, p. 410).

2. **The presence within the alveoli of fibrinous exudation and leucocytes.**—This is less frequent than the preceding (Fig. 201). The exudation-products are similar to those which fill the alveoli in ordinary croupous pneumonia (Fig. 190, p. 512). The coagulum, however, is usually not so abundant, neither is the fibrillation quite

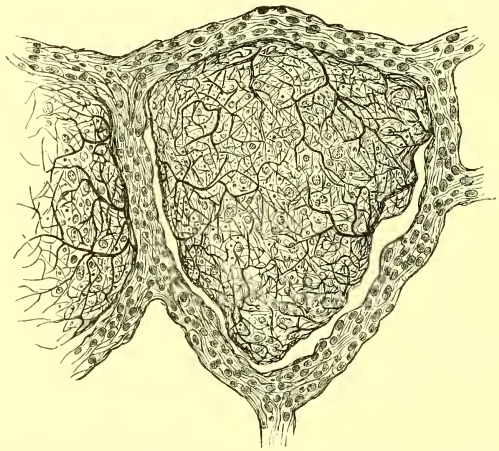


FIG. 201.—*Acute Phthisis.* Showing one of the alveoli filled with fibrinous exudation and leucocytes, and some cellular infiltration of the alveolar wall. × 200.

so distinct. In the most acute forms of phthisis, this may constitute the principal cause of the pulmonary consolidation, but it is usually associated with more or less epithelial proliferation.

The appearances presented by the lungs, in those cases in which the pulmonary consolidation is due *mainly* to any of the *intra*-alveolar changes above described, are very characteristic. The consolidated tissue is soft and friable, breaking down very readily under the finger, and there is complete absence of any induration. The consolidation, although sometimes almost uniform, generally presents a somewhat lobulated outline, indicating the implication of different groups of the pulmonary lobules (p. 518). The colour varies from a reddish to a

yellowish-grey; while small portions of a more decidedly yellow tint are often scattered through the consolidated mass. These scattered areas correspond with those parts in which the retrogressive changes are the most advanced, and they are even softer in consistence than the surrounding tissue. In many parts, the consolidated tissue will be found broken down, so as to form cavities of various sizes. These usually possess irregular walls, which are quite soft and friable, like the solid tissue surrounding them.

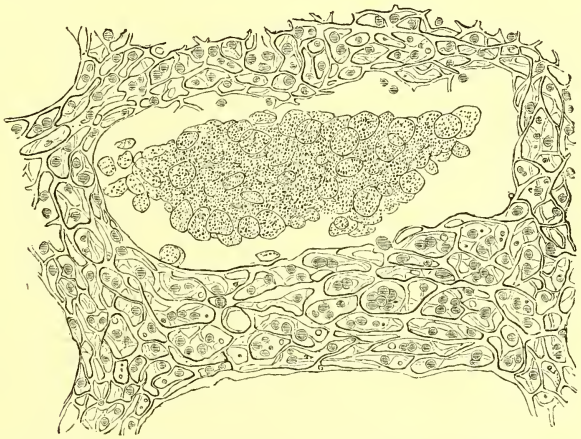


FIG. 202.—*Section of Lung from a case of somewhat Chronic Phthisis.* Showing the thickening of the alveolar walls by a fibro-nucleated tissue resembling lymphoid tissue; together with an accumulation of epithelial cells within the alveolar cavity. The latter are undergoing retrogressive changes. × 200.

3. **A cellular infiltration and thickening of the alveolar walls**, and, in most cases, of the walls of the terminal bronchioles. This is the most characteristic phthisical lesion; for while it is *constantly* associated with the above *intra*-alveolar changes, it is only *exceptionally* present in the more acute pulmonary inflammations previously described. Its extent varies considerably in different cases. The change is precisely similar to that which has been already described as occurring in acute miliary tuberculosis (p. 411). In its earlier stages, a few small cells are seen infiltrating the alveolar septa, which are thus slightly thickened (Figs. 199 and 201). As the change proceeds, the number of these cells increases, and from them an imperfect fibro-nucleated structure is developed (Fig. 202). This

structure is always imperfectly supplied with new blood-vessels. As the new tissue develops in the alveolar walls, it gradually obliterates and replaces the alveolar cavities; so that whilst in some portions the thick-walled alveoli may be found still containing epithelial elements, exudation-products, or even giant-cells, in others, large tracts will be seen, consisting almost entirely of the small-celled growth. The development of this new non-vascular tissue in the alveolar walls leads to the partial, or even complete, obliteration of the pulmonary capillaries, which, as will be seen subsequently (p. 538), constitutes an important element in the causation of the retrograde changes.

The changes, which may subsequently take place in this alveolar growth, vary. The infiltrated septa may rapidly break down before any marked thickening or development of new tissue has had time to occur; whilst in other less acute cases, there is a considerable development of the imperfect fibro-nucleated tissue. Yet, although this may remain as a more or less permanent structure, it usually undergoes in its turn retrogressive metamorphosis (p. 537). These two kinds of change are very often found simultaneously in the alveolar walls of different parts of the same lung. In those portions in which the new tissue is undergoing *degeneration*, it will be seen to have become converted into a structureless granular débris, together with any cells which may be contained within the alveoli; whilst, in the immediate vicinity of these degenerated portions, a more permanent *fibro-nucleated structure* may be found.

Respecting the alteration which the growth of this small-celled tissue produces in the physical characters of the lungs—it may be stated generally that it usually leads to more or less induration of the pulmonary texture. The extent of this induration will vary according to the characters of the new tissue. If the tissue remain almost entirely cellular—as is the case when it is very rapidly formed, and when new vessels do not develop—it will produce little or no induration of the pulmonary consolidation: and this consolidation, consisting mainly of degenerating cells both in the walls and cavities of the alveoli, will be soft and friable in consistence, much resembling that already described. When, on the other hand, as is more frequently the case, there is any considerable development of the imperfect fibro-nucleated growth, when the reticulum is dense and abundant, and when vessels develop and persist, there will be a corresponding induration of the consolidated tissue. In many cases, these changes produce uniform tracts of indurated consolidation of a greyish colour

mottled with black pigment. Scattered here and there among them, may be seen yellowish patches corresponding to the portions which have undergone retrogressive fatty changes.

4. **An increase in the interlobular connective-tissue.**—This is met with, to a greater or less extent, in all the more *chronic* forms of phthisis. This tissue, which surrounds the bronchi and blood-vessels, and contributes to the formation of the alveoli, is found not only increased in amount, but also altered in character. In the earlier

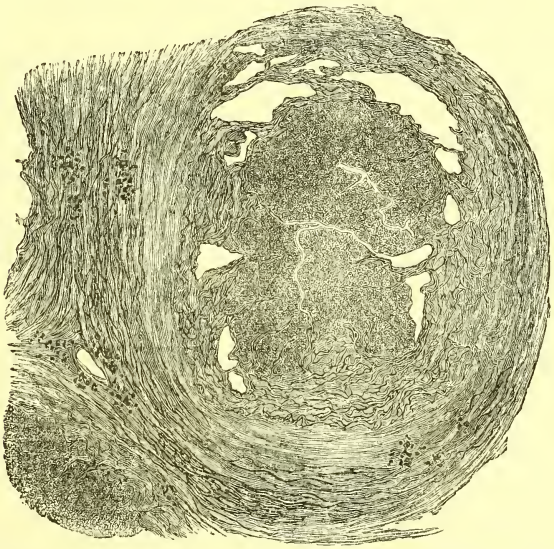


FIG. 203.—*Chronic Phthisis.* Showing the new interlobular fibroid growth surrounding and encapsulating a degenerated and caseous portion of the consolidated lung. × 50. Reduced ½.

stages of its development, it contains numerous small cells; and although many parts of it may resemble the growth in the alveolar walls, its structure is more like that met with as the result of chronic indurative processes in other organs. It has a much greater tendency to become developed into a fibroid tissue than the interalveolar growth, and it is rarely the seat of those retrograde changes which are so frequent in the tissue originating in the alveolar walls. As usually met with, it consists either of wavy fibres or of a more or less reticulated structure, with a varying number of round, spindle-shaped or branched cells (Fig. 203). Intermingled with these, in most cases, are granules

of black pigment. These differences in the pathological tendencies and structure of the interalveolar and interlobular growths vary with corresponding differences in the amount of their vascular supply. Whereas in the *interalveolar* growth, the pulmonary capillaries become obliterated and new vessels are rarely formed, or if formed, are often subsequently destroyed; in the *interlobular* growth, the new vessels formed generally persist. In the most chronic cases of phthisis, this interlobular fibrous growth may constitute the predominant structural change, and large tracts of the pulmonary texture may be found completely replaced by it (p. 523).

An increase in the interlobular connective-tissue in phthisis—inasmuch as the new tissue tends to become dense and fibroid—leads to extensive induration of the pulmonary texture; and further, owing to the contraction which the new tissue undergoes, its growth ultimately produces a corresponding contraction of the diseased lung. In all those cases of phthisis in which there is either a marked thickening of the alveolar walls, or an increase in the interlobular connective-tissue, any cavities which may exist in the consolidated and indurated tissue are characterised by the tough and fibroid structure of their walls. These present a marked contrast to the soft friable tissue surrounding the cavities in cases where the pulmonary consolidation is due mainly to intra-alveolar changes.

Changes in the Bronchi.—Allusion must now be made to certain changes in the bronchi. These tubes are invariably involved in pulmonary phthisis. Some catarrh of the bronchi is constantly present in phthisical lungs. The catarrh is sometimes general, but much more commonly it is limited, and more strictly confined to such portions of the lung as are becoming, or have already become, consolidated. In many cases there is a marked tendency of this bronchial catarrh to lead to extensive cell-infiltration of the deeper structures of the bronchial wall. This cell-infiltration sometimes leads to the production of small ulcers. These have thickened opaque edges, and when once formed they tend to increase. In addition to these changes in the bronchial mucous membrane, there is often a cellular infiltration of the peribronchial tissue, and here small nodules of new growth are frequently met with—especially round the smallest bronchi.

Changes in the Arteries.—Bands of tissue containing arteries frequently extend from side to side of a large cavity. When such an artery traverses a newly-formed cavity, it generally happens that inflammation of the walls of the vessel leads to thrombosis and

subsequent obliteration of the lumen before the advancing disease can destroy its walls and give rise to hæmorrhage. But occasionally, in the case of a small cavity, the wall of the vessel may be weakened at one spot, and an aneurysm result before any thrombosis has occurred. Such an aneurysm may fill the cavity and for a time increase *pari passu* with it. But before such an aneurysm has attained a diameter of an inch, it will, in all probability, rupture; and fatal hæmorrhage into the air-passages may follow.

PATHOLOGY.—Having thus briefly described the various structural changes met with in the lungs in phthisis, there remains to be considered the nature of the morbid processes upon which they depend. In the first place, it is evident that these changes are structurally analogous to those we have met with in the several forms of pulmonary inflammation. Thus the exudation of fibrin and leucocytes, the accumulation of epithelial cells within the alveoli, and, in the more chronic cases, the ultimate infiltration of the alveolar walls are the usual lesions found in croupous and catarrhal pneumonia; while an increase in the interlobular connective-tissue is the characteristic change in interstitial pneumonia. These considerations, together with others derived from the study of the ætiology of the disease, are sufficient to justify the conclusion that the morbid processes, which lead to the consolidation and subsequent disintegration of the lung, come within the category of **inflammation**, and that the differences in the histological changes to which they give rise are due mainly to differences in the nature of the irritant, and in the duration of the inflammatory process.

But although phthisical consolidation of the lung is the result of inflammation, it is obvious from our previous considerations (p. 292), that the process does not owe its origin to "simple" causes. The *progressive* character of the inflammation, and its tendency to infect adjacent and distant portions of the lung, show the existence of some irritant capable of multiplying in the body and of spreading from primary to secondary foci. Since Koch's discovery of the tubercle bacillus, all investigations have tended to show that the bacillus tuberculosis is invariably present, both in the lungs and in the sputum, in all cases of phthisis (Fig. 204); and we must therefore regard phthisis as a more or less

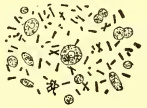


FIG. 204.—*Tubercle Bacilli.* In phthisical sputum. × 300.

chronic **pulmonary tuberculosis.** Thus modern opinion agrees with Laennec in believing that all phthisis is tubercular, and with Niemeyer in his conclusion that phthisis is a progressive caseous pneumonia.

To understand the differences in the histological changes just described, it is important to bear in mind what has been stated respecting the variations in the character of the structural alterations in inflammation, produced by differences in the intensity and duration of the inflammatory process. When studying the process of inflammation, it was seen that the most intense forms of the process were characterised by abundant fluid and corpuscular exudation; whereas in inflammations of less intensity and longer duration, tissue-formation played a prominent part. These structural changes also varied according to the duration of the inflammation. In the least severe and most chronic forms, there was a tendency for the changes to be limited to the elements immediately adjacent to the blood-vessels and lymphatics, whereas in inflammations of somewhat greater intensity, more distant elements became involved. Further, whereas in the former case, the changes usually resulted in the formation of a small-celled tissue which tended to become fibroid, in the latter, the more distant elements—being in most cases incapable of further development—tended to undergo retrogressive changes. In the lungs, the truth of these propositions was borne out by the differences which were seen to exist in the histological characters of the lesions in the various forms of pulmonary inflammation, and also of those in acute tuberculosis.

If the above facts be kept in view, it will be seen that the same sequences characterise the lesions in pulmonary phthisis. In those cases in which the inflammatory processes are of slight intensity and of long duration, the most marked structural change will consist in the development of a small-celled growth in the alveolar walls, and in the interlobular tissue—a growth which tends to develop into a fibroid structure; whereas in those cases in which the inflammation is of greater intensity, fluid and corpuscular exudation, and proliferation of the alveolar epithelium, will constitute more prominent parts of the process.

The intensity of the inflammatory process not only determines the histological characters of the pulmonary consolidation, but also, to a great extent, the subsequent changes which take place in it. In those cases of phthisis in which the intensity of the inflammatory process is considerable, not only do the epithelium and exudation-products, which have accumulated within the alveoli, quickly degenerate

and break down, but any small-celled tissue, which may have been developed in the alveolar walls or around the terminal bronchioles, also softens and dies, and thus the vitality of large tracts of the pulmonary consolidation may become destroyed. In those cases, on the other hand, in which the process is less intense, the small-celled growth produced in the alveolar and bronchial walls is more permanent, and there is an increase in the interlobular connective-tissue. It is these two kinds of change, the one tending towards death, and the other towards the production of new tissue, which produce the caseation and softening on the one hand, and the induration on the other; and these again, associated in such various degrees, make up the diverse physical characters of the phthisical lung, and have given rise to a classification of phthisis into *ulcerative* and *indurative* varieties.

These various **secondary changes** which may take place in the pulmonary consolidation of phthisis must be considered more fully. They are of three kinds—resolution, development into an imperfect fibroid tissue, and retrograde metamorphosis.

Resolution.—Much of that consolidation of the lung which is the most rapidly induced, and which is consequently owing to the presence of intra-alveolar exudation, may become absorbed. The resolution of the consolidation may thus be complete; or after the absorption of the intra-alveolar products there may remain more or less infiltration of the alveolar walls.

Fibroid development.—This, as has been seen, may succeed the growth in the alveolar walls, and also form the new interlobular tissue. The tissue which originates in the walls of the alveoli, being for the most part destitute of blood-vessels, is incapable of forming a very mature structure, but it may develop into an imperfect tissue, and remain for some time permanent, thus contributing to the induration of the lung. In the new interlobular tissue there is not the same interference with the vascular supply, and hence this forms a much more fully developed and permanent structure, and is the principal source of the pulmonary fibrosis. The extent of this fibrosis is, for the most part, in direct proportion to the chronicity of the disease.

Retrograde metamorphosis.—This is the change which, leading to the caseation, softening, and disintegration, so characteristic of phthisis, distinguishes phthisical from other forms of pneumonic consolidation. A retrograde change in the inflammatory products is an invariable accompaniment of acute non-phthisical pneumonia. Much

of the exudation and epithelium which fill the alveoli undergoes fatty and mucoid changes, and as the circulation becomes restored in the pulmonary capillaries, the degenerated products are absorbed, and the lung remains intact. In phthisical consolidation, however, this removal of the inflammatory products does not take place. The contents of the alveoli degenerate, but the degenerated products are not absorbed, and the lung-tissue itself undergoes a rapid or gradual process of disintegration.

In studying the causes of this retrograde metamorphosis, which constitutes so essential a feature of the disease, we find that it has usually been attributed to conditions interfering with the circulation. The most important of these are (1) the pressure upon the small blood-vessels of the new cells infiltrating the walls of the alveoli and small bronchi; (2) the pressure exercised upon the pulmonary capillaries by the inflammatory products which have accumulated within the alveoli; and (3) that tendency to stagnation of the blood-stream which is an invariable accompaniment of every intense inflammation.

This explanation is, however, clearly insufficient, as all these conditions may exist without producing the degeneration and softening shown to be so characteristic of phthisis. The death, degeneration and caseation seem to be mainly due to the direct action of the products of the bacillus. The new cells are thus often killed before vessels would normally develop among them; while the original tissues gradually succumb as the products of the advancing organisms act more and more powerfully upon them. The organism and its products are everywhere met by inflammatory changes. What determines the successful development of fibroid-tissue, how far its formation depends upon the nature of the tissue attacked, and how far upon the vitality of the invading organism, is uncertain. These difficulties have been already discussed (pp. 321, 400, 403). The development of fibroid-tissue is a favourable result in two ways: it is evidence of the recuperative power of the tissues, and it forms a barrier against the advance of the bacillus.

In addition to the above, an element of probable importance in the causation of the retrograde changes of phthisis is *inherent weakness* of the lungs (possibly inherited), which not only renders them especially susceptible to injury, but which reduces their recuperative power to a point below the normal average.

In the later stages of many cases of chronic phthisis, secondary inflammation and ulceration of the pulmonary consolidation con-

tribute to the destruction of the lung. These result from the injurious influence of retained secretions and inflammatory products, which may contain other organisms—such as the streptococcus pyogenes—besides the bacillus tuberculosis.

ÆTIOLOGY.—In studying the ætiology of phthisis, it is obvious, in the first place, that, accepting the tubercle bacillus as an essential element, something more is necessary for the production of the disease. The bacillus, as has been seen, must in some situations be constantly entering the lungs by means of the respired air (p. 398). In hospitals set apart for the treatment of consumption, the sources of infection abound, yet the instances in which phthisis develops in the typically healthy are rare. The other necessary factor is something inherited or acquired—**inherent in the individual**.

The influence of **hereditary predisposition** is so marked that it must necessarily occupy a prominent place in the pathology of phthisis. As to the nature of what is transmitted—although in quite exceptional cases this may possibly be the tubercle bacillus—speaking generally, it is in all probability simply a tendency to disease. It may be said that this tendency consists in some feebleness of the constitution in general, and often of the lungs and other organs in particular. As a result of this feebleness, the power of resisting injurious influences is diminished, and the lungs and often other organs and tissues which are especially weak are, in consequence, abnormally liable to become suitable culture-grounds for the bacillus tuberculosis. Further—this inherited weakness not only renders certain organs abnormally liable to invasion, but also less capable of recovering from the effects of the consequent inflammatory process.

Another important factor in the development of phthisis is the state of the **general health**. Quite apart from any inherited feebleness, there can be no doubt that an impaired state of the general health greatly favours the development and progress of the disease. It is when *both* these obtain that we have the most favourable conditions. Dampness of soil and atmosphere, want of sunlight, and lack of *fresh* air, seem to contribute especially to the production of this "impaired health."

In these two conditions, therefore, *hereditary predisposition* and *state of general health,* we have the other factor—the something inherent in the individual which appears to be necessary for the production of phthisis. It is this **inherent** condition which must be

regarded as constituting a soil favourable to the development of the bacillus, and, whatever it may be, its importance is difficult to over-estimate.

Attention has already been drawn to the frequency with which phthisis commences in the apices of the lungs. The causes of this are probably to be sought for in the diminished range of respiratory movement which obtains in the highest portions of the lungs. As a result of this diminished movement, there is diminished aëration of blood, and, in certain conditions of health, a tendency to stagnation of the blood-stream in the pulmonary capillaries. The stagnation of the circulation may lead to more or less injury of the walls of the vessels, and a slight leakage be thus induced.

It is obvious that any inherited or acquired weakness must favour the occurrence of these apical changes. General feebleness and want of vigour lead to loss of muscular strength and weakness of the heart, and thus tend to prevent the full expansion of the chest, to cause a stooping posture of the body, and to impair the blood and air-circulation—all conditions favouring blood-stagnation in the highest portions of the lungs. Further, the success which attends residence in a rarefied atmosphere is probably dependent on the increased rhythmical expansion of the lungs.

CHAPTER XXXII.

PATHOLOGY OF THE CENTRAL NERVOUS SYSTEM.

The central nervous system is made up of *cells* and their *processes,* and of a connective-tissue *neuroglia* with blood-vessels and lymphatics. The Golgi method has demonstrated that every nerve-cell has *one nerve* process, termed the axis-cylinder process or *neuron,* which gives off collaterals, and, after a short course from the cell, is covered with myelin. The myelin sheath remains until near the termination of the neuron, which breaks up into a brushwork of fibrils in the neighbourhood of other nerve-cells. A number of other processes arise from the ganglion-cell termed *dendrites,* which, projected into corresponding lymph spaces, serve to absorb nourishment for the cell (Fig. 205).

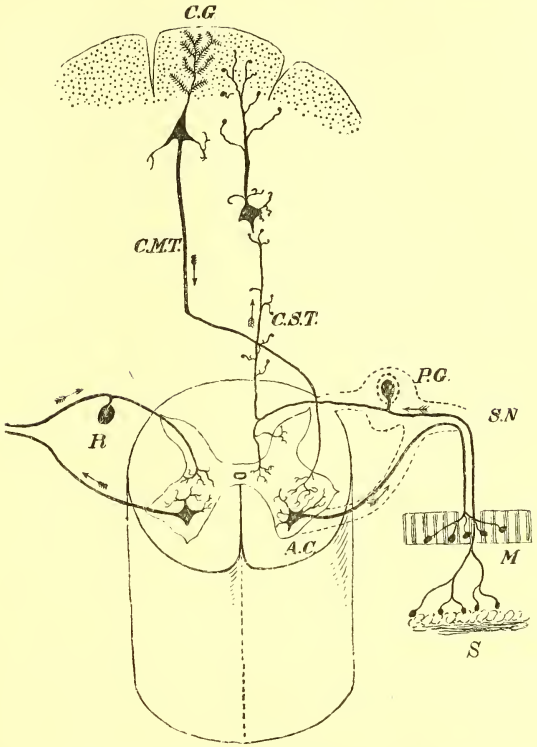


FIG. 205.—*Diagrammatic representation of the Motor (Efferent) and Sensory (Afferent) Tracts. (After Ramon y Cajal.)*

THE EFFERENT TRACT.—*C.G.* is a pyramidal cell of the cortex of the motor area with its nutritive protoplasmic processes or dendrites. From the centre of the base of the cell is given off the neuron or axis-cylinder process, *C.M.T.*, which decussates in the pyramids and terminates in a brushwork of fibrils in the anterior cornu, *A.C.*, where it is brought into physiological connection with a spinal motor cell. This is also represented as having protoplasmic processes and one axis-cylinder process or neuron, which passes out by the anterior root to terminate in a motorial end-plate of a muscle-fibre, *M.*

THE AFFERENT TRACT.—A ganglion on the posterior root, *P.G.*, gives off a T-shaped process, one branch going to the periphery to terminate in an end-organ or plexus; the other enters the posterior column of the spinal cord; some fibres pass into the grey matter of the posterior horn. Thence the impulses are conveyed onwards by fresh neurons arising from cells in the grey matter, while other long fibres continue their course onwards to the brain, *C.S.T.*, by the posterior column of the same side. The leg-fibres enter *Goll's nucleus*, the arm-fibres, *Burdach's nucleus*. From the ganglion-cells of these nuclei the upward path to the *cortex* after decussation in the medulla is by the fillet of the opposite side, probably in the optic thalamus. *R* represents a *simple reflex arc* consisting of an afferent nerve derived from a posterior spinal ganglion-cell terminating in the neighbourhood of an anterior horn-cell, from which an efferent fibre is given off.

The neuroglia consists of fine fibrils and branched cells, termed *glia*-cells. It serves to hold the nerve-cells and their processes together, and to carry the blood-vessels and lymphatics.

The *grey matter* consists of ganglion-cells and their processes, and neuroglia. The *white* matter consists of axis-cylinders covered with myelin, to which it owes its colour, the nerve-fibres being held together with neuroglia. The *grey matter* has a pink tint, which offers a striking contrast to the dead white of the *white matter:* the difference is accounted for by the much greater vascularity of the former.

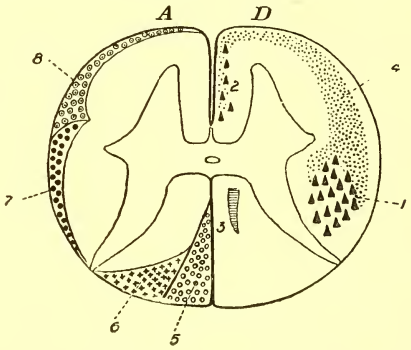


FIG. 206.—*Scheme to represent the ascending and descending degenerations in transverse lesions of the spinal cord. A.* Ascending; *D.* Descending. 1. Crossed pyramidal tract; 2. Direct pyramidal tract; 3. Comma-shaped tract; 4. Intermediary bundle of the lateral column; 5. Goll's column; 6. Burdach's column; 7. Direct cerebellar; 8. Antero-lateral. Lissauer's tract at the base of the posterior horn is not shown. The root zone (bandelette of Charcot) is the portion of the posterior column between Burdach's column and the posterior horn. (F. W. Mott, after Marie.)

Nerve-fibres may be divided into three systems.

(1) *Afferent* or sensory—those which conduct impulses from the periphery to the central nervous system.

(2) *Efferent*—those which conduct impulses from the central nervous system to the periphery (Figs. 205 and 206).

(3) *Intra-central Commissural.*—(1) Fibres which run *transversely,* uniting the two halves of the central nervous system—*e.g.,* the corpus callosum, the middle cerebellar peduncle, and the anterior and posterior commissures of the spinal cord, &c.; (2) fibres which run *longitudinally—e.g.,* association-fibres of the cerebral hemispheres, and the ground fibres (ascending and descending) of the spinal cord.

The normal and morbid anatomy of the central nervous system is in great measure founded upon the discovery of Waller, that a nerve-fibre is dependent for *its nutrition* upon the nerve-cell, of which its axis-cylinder process is an outgrowth. The series of changes which occur in a nerve-fibre of the peripheral or central nervous system, when cut off from its seat of nutrition experimentally or by disease, is termed **Wallerian degeneration**.

The methods employed for studying Wallerian degeneration of the central nervous system, taking (for example) the spinal cord, where the afferent and efferent tracts are clearly defined, are as follows:— If posterior spinal roots be cut, or there be a transverse lesion of the spinal cord, it would be possible, after ten days have elapsed, to recognise naked-eye changes in definite tracts of the spinal cord, provided the spinal cord be suspended in Müller's fluid for a month or so. The cord thus hardened is cut transversely and the degenerated tracts are recognised by their *lighter yellow colour*, as compared with the healthy white matter which is now stained a brownish yellow. For microscopical examination of such an early degeneration, there is no method to compare with that of Marchi. It consists in placing thin transverse slices of the central nervous system thus hardened, in a solution of *one* part of a one per cent. solution of osmic acid and *two* parts of Müller's fluid for a week, then washing with water and cutting by the celloidin method. Sections should be cut longitudinally and transversely. The early changes in the axis-cylinder and myelin sheath are beautifully shown, and even single degenerated fibres can be followed the whole length of the spinal cord. The healthy fibres are stained a light grey by the osmic acid, but both the axis-cylinder process and the breaking-up myelin are stained *black*, owing to fatty degeneration. This method is most suitable for *early* degenerations one week to one month after the lesion. For *later* degenerations, the Weigert or Weigert-Pal methods are most suitable. When sclerosis has taken place, it is better to adopt one of the latter methods; the healthy white matter is then stained blue, and the *sclerosed* tissue is yellow or unstained, according to the method adopted. Wallerian degeneration of the nerve-fibres of the central nervous system must occur in all organic lesions, and its extent and distribution will depend entirely upon the ganglion-cells destroyed, or upon the fibres which have been interrupted in their continuity with the cells of which they are outgrowths. The morbid conditions which may give rise to Wallerian degeneration may be then classified into three headings:—

(1) **Inflammatory lesions**, circumscribed or diffuse: these will include meningitis, encephalitis, abscess, myelitis circumscribed or diffuse.

(2) **Local diseases**, due to ischæmia, to softening produced by embolism or thrombosis, and to hæmorrhage—causing secondary degenerations, but not necessarily inflammation except at the seat of injury.

(3) **Primary degenerations.**—It is a debatable question whether the chronic inflammatory changes, which are always associated with these systemic degenerations, are secondary to the atrophy of the nerve fibres, or whether they are primary and therefore the cause of the degeneration. The opinion is steadily gaining ground that the primary cause is a retrogressive nutritional change in the ganglion-cells—consequently there is a progressive degeneration of their axis-cylinder processes commencing at their terminations.

The microscopical changes in the fibres, as a result of degeneration, are a breaking-up of the myelin sheath (there is no neurilemma), an alteration in its chemical composition, and swelling of the axis-cylinder process owing to a fatty degeneration; the clear distinction between the central axis-cylinder and surrounding myelin thus being lost. Later, as the altered myelin is carried away by phagocytes, spaces may be seen with the swollen axis-cylinder in the middle; or empty spaces in the neuroglia tissue occur owing to rupture and absorption of the degenerated axis-cylinder processes (Figs. 207 and 208). As the atrophy of the nervous structures proceeds, there is a hyperplasia of the neuroglia, and proliferation of the glia-cells. The process during the early stages has been one of softening; it is now a true **sclerosis** with shrinking, but there is no tendency (in uncomplicated *primary* or *secondary* systemic degeneration) for the sclerosis to extend its limits, and it may even be limited to a microscopic transverse area. The connective-tissue overgrowth shuts off its own nutrition by changes in the walls of its nutrient vessels. Eventually a cicatricial tissue may be formed; and the presence of this impenetrable tissue may be the reason why in the higher animals there exists no definite proof that *regeneration* of nerve-fibres can take place in the central nervous system.

Some of the **physiological effects of degeneration** of the central nervous system are voluntary *paralysis* when the upper segment of the motor path is degenerated, and paralysis with wasting and degeneration of muscles when the lower segment is affected. When

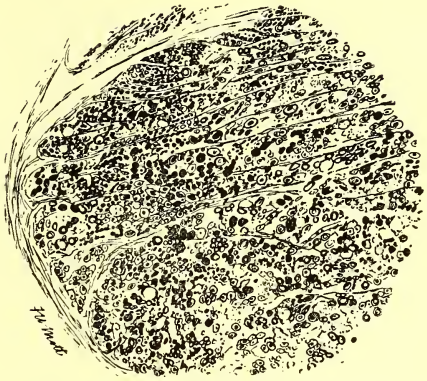


FIG. 207.—*Degeneration of crossed Pyramidal Tract at the 10th Dorsal Segment*, forty days after hemisection of the spinal cord in the mid-dorsal region. The drawing was made from a photo-micrograph of a section of the posterior part of the lateral column, stained by the Pal method. The condition is one of commencing sclerosis. The black dots are the swollen axis cylinder processes, mingled with the degenerated myelin; here and there are parts unstained, showing that the nerve fibres have disappeared and neuroglia alone is left. A few empty spaces are seen scattered about, showing the previous existence of nerve fibres at these points. A large number of healthy fibres are seen mingled with the degenerated fibres; these are the fibres of the direct cerebellar tract on their way to the periphery of the cord. (Mott, *Phil. Trans.*, 1892.)

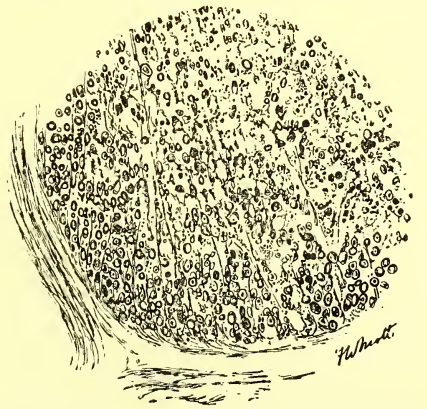


FIG. 208.—*Degeneration of Crossed Pyramidal Tract at the 8th Dorsal Segment*, seventy days after hemisection of the spinal cord in the mid-dorsal region. Prepared and drawn in the same way as Fig. 207. Much more *sclerosis* and *atrophy* is seen. The degenerated nerves have for the most part disappeared, empty spaces in the neuroglia being left; some few black dots are shown—indications remaining of degenerated nerve fibres. At the periphery the healthy fibres of the direct cerebellar tract are seen. (Mott, *Phil. Trans.*, 1892.)

the afferent tract is degenerated, sensory disturbances occur—*e.g.*, loss of the muscular sense, thermo-anæsthesia, analgesia, tactile anæsthesia, and hyperæsthesia. Sometimes tactile and painful impressions may produce tingling or thrilling sensations—this perverted sensation has been termed paræsthesia or dysæsthesia. When an impression on one part of the body is referred to a similar spot on the opposite side, the condition is known as allocheiria: it occurs especially in affections of the posterior columns of the cord.

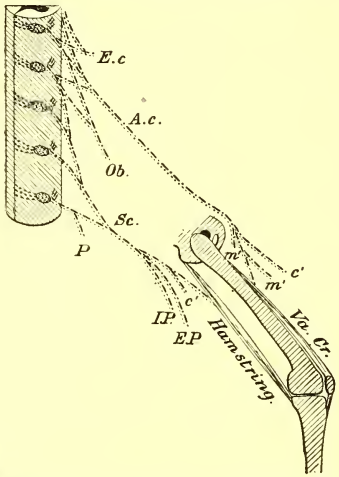


FIG. 209.—*Diagram to Explain the Knee-jerk* (Sherrington). *E.c.* External cutaneous nerve. *A.c.* Anterior crural nerve with *c'* cutaneous, and *m'* muscular branches, coming from the 3rd and 4th lumbar segments of the spinal cord. *Ob.* Obturator. *Sc.* Sciatic nerve with *I.P.*, internal popliteal. *E.P.* External popliteal branches. *Va. Cr.* The vasti and the crureus muscles, the internal portion being especially concerned in the knee-jerk. Destruction of the reflex arc of the 3rd and 4th lumbar segments in either its efferent or afferent portions will abolish the knee-jerk, because it will either paralyse the vastus crureus muscle or destroy its "myotatic" irritability.*

Changes in the superficial and deep reflexes.—Both superficial and deep reflexes are usually exaggerated when the pyramidal tracts are degenerated, showing that the cerebral cortex of the motor area, from which these fibres originate, exerts an inhibitory influence upon the simple spinal reflex acts.

The knee-jerk is the best example of a so-called deep reflex, but although dependent upon the integrity of the reflex arc of the fourth and third lumbar segments of the spinal cord, yet careful time-measurements have shown that it is not a reflex. It is produced by striking the quadriceps tendon *put on the stretch* by flexing the knee, and thereby at the same time relaxing the hamstring muscles, which Sherrington has shown to have a correlative antagonistic action to the quadriceps. This is not, however, so much due to the fact that relaxation of the flexor muscles of the knee leaves that joint more free to move when the quadriceps

* *Myotatic irritability* is the term used by Gowers to embody his view that the knee-jerk and other deep reflexes depend on the increased irritability of a *stretched* muscle. If the tension is sudden and forcible, not only increased irritability but visible contraction occurs. This is especially evident when cerebral influence has been removed by pyramidal degeneration.

extensor is excited to contraction by tapping its stretched tendon, as to the removal of an antagonistic tonic influence through afferent nerves (fifth and sixth lumbar roots), which the flexor group of muscles exert through the spinal reflex arc upon the correlated extensor group (Fig. 209). Absence of the tendon reflex without wasting and degeneration of muscle, indicates degeneration of the posterior columns of the cord. Absence of the tendon reflex with wasting of muscle and sensory disturbance, indicates peripheral nerve degeneration or destruction of central grey matter of anterior and posterior horns. Absence of the tendon reflex with wasting and degeneration of muscle, but without sensory disturbance, indicates degeneration of the anterior horn cells or primary progressive myopathy.

By muscular degeneration is not meant disuse-atrophy, but a wasting accompanied by changes in electrical excitability of the nerve and muscle. Bastian has pointed out that complete destructive transverse lesions of the spinal cord high up in the dorsal or cervical regions (and in which *presumably* therefore *the reflex arc is intact*) are often followed by absence of the knee-jerk. Of course the pyramidal tracts will be degenerated, and it is difficult therefore to understand why the knee-jerks are lost. It cannot be explained by the removal of cerebellar influence; for the statement of Marchi, that there exists a descending cerebellar tract, has been disproved. The knee-jerk is diminished in old age, during sleep, and in anæmia of the spinal cord.

In cases where the knee-jerk is exaggerated from removal of cortical influence by degeneration of the pyramidal tracts, another phenomenon is often obtainable, namely, if the calf-muscles which extend the ankle-joint are suddenly put on the stretch by pressing the hand against the sole of the foot, a quick contraction occurs, and by keeping up the pressure there is a recurrence of the contractions at a regular rate (about eight per second); the foot is thus thrown into a series of clonic spasmodic contractions termed the *foot clonus* or *ankle clonus*. Conditions which give rise to ankle clonus are usually accompanied or followed by *contracture*, a state of permanently increased muscular tonus.

Examples of *reflex spinal tonus* are also afforded by the action of the sphincters of the bladder and rectum. The tonic contraction of these muscles is abolished by destruction of the lumbar enlargement of the spinal cord—hence incontinence of fæces and urine.

INFLAMMATION OF THE MENINGES.

Three membranes enclose the central nervous system, but owing to the intimate connection of the pia mater and arachnoid, these always

suffer together. Inflammation of the tough fibrous *dura mater* is termed *Pachymeningitis*. Inflammation of the soft *pia-arachnoid* is termed *Meningitis*, or more precisely, as the antithesis to pachymeningitis, *Leptomeningitis*.

Pachymeningitis.

The dura mater consists of two layers, a thick outer layer which is periosteal in its functions, and a thin inner layer with a smooth epithelial surface. Either layer may be the seat of inflammation, which is usually chronic.

External Pachymeningitis is frequently caused by caries or necrosis of the bones of the skull due to syphilis or wounds.

Internal Pachymeningitis is characterised by the formation of a false membrane, usually very vascular and consisting of several superimposed layers. Owing to rupture of vessels, blood-cysts are found between the layers, known by the name of *hæmatomata* of the dura mater. This membrane, which usually causes adherence of the dura mater to the arachnoid, extends generally over the greater part of one or both hemispheres. It is rare, and met with usually in general paralysis of the insane and chronic alcoholism.

Meningitis or Leptomeningitis.

Inflammation of the pia-arachnoid is in nearly all cases due to infective inflammation by micro-organisms. The most important form is tubercular (p. 404). A number of other causes of infection exist, which may be considered under the headings local and general.

Local.—(1) Traumatic injuries of the head with direct infection.

(2) Adjacent disease outside the dura mater, suppurative otitis, chronic ear disease with caries of the mastoid or petrous portions of the temporal bone, and occasionally disease of the bones of the nose or orbit. The infection in these cases may spread directly, or along the course of lymphatics or blood-vessels.

(3) Tumours and abscesses of the brain may cause adjacent inflammation of the meninges.

General.—Meningitis may occur in the course of certain infective diseases—*e.g.*, small-pox, scarlet fever, measles, septicæmia, and in pneumonia and acute rheumatism. Cerebro-spinal meningitis may also occur in an *epidemic form*. Meningitis in rare instances has followed a blow not causing any wound, and it has been found post-mortem in some cases of sunstroke.

Morbid Anatomy.—When the infection is local the meningitis may be circumscribed, but when the cause is some infective blood condition it is usually generalised, and may in some cases affect the spinal as well as the cerebral meninges—*e.g.*, meningitis occurring in the course of pneumonia may in many ways resemble the epidemic form. Tubercular meningitis usually affects *the base* primarily and especially, whereas in other forms the *convexities* of the hemispheres are affected. Certain changes are common to all forms of meningitis. The pia mater is intensely hyperæmic and red, as if the vessels had been artificially injected. Soon opacity and thickening of the membranes occur, recognisable most readily in the arachnoid; and along the course of the vessels there is an opacity owing to distension of the perivascular lymphatic sheaths. An inflammatory exudation from the blood-vessels of the pia mater occurs: this may be serous, sero-purulent or purulent, and is manifest especially over the sulci of the convexity and the spaces at the base of the brain. In severe cases pus mixed with fibrin forms a continuous opaque yellowish layer under the visceral layer of the arachnoid. The inflammation usually spreads to the adjacent structures, causing neuritis, encephalitis, and, later on, adhesions. The ventricles of the brain and the inter-peduncular subarachnoid space may be distended with a turbid serous fluid, and the choroid plexus as well as the velum interpositum are usually congested and swollen. This fluid, examined microscopically, may be found to contain large granular epithelial cells, leucocytes, or pus cells.

The suppurative process is extremely marked, and often very rapid in formation in epidemic cerebro-spinal meningitis.

Pathology.—The first stage, or *period of excitation,* is characterised by *headache, delirium, rigidity, general or local convulsions,* and these symptoms can be accounted for by the general hyperæmia of the cortex cerebri.

The second stage or *period of depression* occurs as the inflammation extends into the cortex and motor nerves, *paralyses* of various kinds appearing. In the final stage, the increasing effusion into the skull and the rising intra-cranial pressure induces *coma.*

INFLAMMATION OF THE CENTRAL NERVOUS SYSTEM.

Encephalitis.—Inflammation of the brain may arise from three causes: traumatic injury, inflammation of adjacent structures, and acute infective diseases—erysipelas, typhoid, typhus and diphtheria.

Strümpell considers that infantile cerebral hemiplegia is due to a primary systemic inflammation of the grey matter of the motor cortex analogous to anterior polio-myelitis, hence he terms it *Polio-encephalitis.* Very probably the two diseases have an identical cause. *Anatomically,* the alteration in the brain tissue which results from acute inflammation is a process of *red softening* (p. 62).

Cerebral Abscess.—The causes may be divided into local and distant. By far the most frequent *local* cause of cerebral abscess is *chronic ear disease.* Inflammation of the middle ear or mastoid cells is often followed by a purulent discharge and *caries of the bone :* not infrequently arrest of the discharge is followed by abscess. Occasionally there may be no bone disease, only suppurative inflammation of the middle ear or mastoid cells ; and in such cases the infection probably passes by the perivascular lymphatics along the veins which connect the tympanic cavity and mastoid cells respectively with the superior petrosal and lateral sinuses. Disease of the nose and orbit, syphilitic caries of other bones, tumour of the brain, and injury, are among the rarer causes of cerebral abscess. *Distant causes* are pyæmia, gangrene of the lung, fœtid bronchitis, bronchiectasis and empyema—all rarely met with.

Morbid Anatomy.—Abscess is usually single, but there may be several, and in pyæmia sometimes many. Owing to ear disease being such a common cause abscess is met with most frequently in adjacent portions of the brain—viz., the temporo-sphenoidal lobe and the lateral lobe of the cerebellum. In nasal and orbital disease it is usually in the adjacent frontal lobes.

The process of *suppuration* commences with inflammatory softening ; cell infiltration increases greatly, replacing and destroying the normal structure. Pus is formed which, in the case of ear disease, is usually of a greenish colour and frequently of fœtid odour and acid reaction. It is made up of pus corpuscles, degenerated cells, fat, cholesterin, hæmatoidin, and micro-organisms, usually staphylococci. The size of the abscess varies greatly, but the average size is between a walnut and a hen's egg. The pus is contained at first in an irregular cavity, and there is a tendency for the abscess to increase by a necrosis of portions of the limiting tissue ; it may thus, by spreading, burst into the lateral ventricles or externally. It may, however, become encapsuled by connective-tissue, and the pus, undergoing mucous degeneration, becomes thick and viscid. It is thought that pus thus encapsuled may dry up and caseate or calcify, or even be completely absorbed leaving little more than a scar.

Myelitis.—The term *myelitis* has been used for all forms of degeneration of the spinal cord, and thus we have the sub-divisions—acute, sub-acute, and chronic; or it may be considered according to its localisation, and then the terms transverse myelitis, diffuse myelitis, leuco-myelitis, polio-myelitis, and meningo-myelitis are used.

The evidence showing that primary myelitis does not occur is accumulating, and the true causes are probably infective organisms or toxic agencies. Cold, injury, &c., may operate, as it does in pneumonia, as a factor in lowering the vital resistance.

Of all the infective diseases which lead to these various forms of myelitis, syphilis is the most important; but tuberculosis (in the production of Pott's disease and meningo-myelitis), epidemic cerebro-spinal meningitis, gonorrhœa, measles, diphtheria, influenza, scarlet fever, small-pox and typhoid, offer examples of infective diseases which have been followed by various forms of myelitis. Probably the inflammation is due to the *toxins* produced in the blood by the infective organisms. Other toxic agencies, such as in ergotism, pellagra and lathyrism, offer examples of *vegetable poisons;* lead and arsenic, of *mineral poisons,* any of which may cause myelitis.

Acute Myelitis.—The naked-eye appearances are variable; the spinal tissue is sometimes softened, pinkish-white in appearance, yellowish or brownish-red, according to the condition of the blood-vessels, and the amount and change in the extravasated red blood-corpuscles (*vide* "Softening," p. 60). Very early one finds a large number of granular corpuscles and amyloid bodies; the axis cylinders are either swollen up, granular, or destroyed, and the myelin sheaths of the white matter are rapidly broken up and destroyed. The ganglion cells undergo degeneration; their processes are seen broken off. In the first stages they become globular and pigmented; they then present signs of atrophy, and eventually may completely disappear.

The *vessels,* thrombosis of which appears in many cases to be the determining cause of the above-mentioned changes, are gorged with blood, and their lymphatic sheaths distended and filled with leucocytes; and when the inflammation is very intense, hæmorrhages may be found. There is an increase of nuclei and small round cells in the grey matter, and the stellate, or Deiter's cells, are more numerous than normal.

Later the connective-tissue undergoes proliferation and there is rapid progressive softening of the nervous elements owing to granulo-fatty degeneration. The process thus passes into the chronic stage con-

stituting *grey softening*. Hæmorrhages may occur in these foci softening, and eventually the process ends in a *sclerosis*.

Diffuse Myelites have a common pathological anatomy, but the clinical symptoms will of necessity vary according to the seat, extent, and distribution of the inflammatory process. In the ordinary acute *dorsal* myelitis phenomena of exaggerated sensibility—such as pain, numbness, and tingling—mark the onset, which is followed by paraplegia and later on by contracture, with exaggerated superficial and deep reflexes, due to the removal of the cerebral influence by degeneration of the pyramidal tracts; there will probably also be wasting of muscles, and the reaction of degeneration, due to destruction of anterior horn cells. The hyperæsthesia and pain is due to inflammation and irritation of the grey matter of the posterior horns, and the *anæsthesia*, which later on replaces the exaggerated sensibility, to destruction of this grey matter and the adjacent commissural white fibres of the lateral column.

Retention of urine and fæces, due to tonic spasm of the sphincters, invariably precedes the *incontinence*.

Trophic troubles, especially *bed-sore* over the sacrum, arise, and these, together with bladder complications, are usually the cause of death. Rapid wasting of the muscles of the leg would indicate the invasion of the *lumbo-sacral* region, also the absence of tonic contraction of the sphincters, the centres of which are situated in this region. Involvement of the arms points to inflammation of the cervical enlargement.

Periependymal, or Central Myelitis, occasionally occurs, but the effects depend, like syringomyelia, upon the amount and seat of destruction of the grey matter.

Meningo-myelitis.—Lately Erb has called attention to the fact that in syphilis, very frequently in the early secondary stage of the disease, a *focal myelitis* occurs characterised by paraplegia, with exaggerated reflexes, girdle sensation, retention of urine and fæces, and other signs of a local transverse lesion of the cord. The disease is rarely fatal, but bed-sores and bladder complications may ensue. In fatal cases no gumma was found, only a transverse myelitis, the principal features of which were diffuse myelitis of the white matter (not involving definite tracts), local thickening of the meninges, and a *periphlebitis*, but no syphilitic changes in the arteries.

Transverse Myelitis, produced by Pott's disease, aneurysm, growths, and thickening of the dura mater. The symptoms are according to the seat of the lesion. The mechanism of the damage to the cord is twofold—viz., *compression* and *inflammation*. The cord may (at the

seat of compression) be flattened, indented, or even reduced very greatly in size; on section it has usually a grey appearance. The microscopical appearances of inflammation correspond to those already described, and the changes in the cord above and below the seat of injury are described under *Secondary Degenerations*.

The pathological effects may be considered under two distinct headings—*Root symptoms* and *Cord symptoms*. The former usually develop first in the form of *shooting pains*, owing to irritation of the sensory roots involved. With the pain there is usually *hyperæsthesia* of the skin. Irritation of motor roots causes *painful contracture*. *Cord symptoms* are: paresis or paralysis below lesions, *increase* of *superficial reflexes* and of *myotatic irritability*. There may be no loss of sensibility discoverable in the parts below the lesion, although there is complete paralysis, but there may, on the other hand, be delay, and in severe cases absolute loss of sensation. The condition of the sphincters and the tendency to bed-sores depend upon the integrity of the lumbar enlargement. If the lesion is in the lower cervical region the pupils may be affected from implication of the cilio-spinal centre, and the pulse rate diminished from damage of the accelerator fibres of the heart.

Polio-myelitis.—An acute inflammation of the anterior cornua is the morbid change which affects the spinal cord in *infantile paralysis* and *acute spinal paralysis* of the adult. Singer and Munzer have shown that they can produce a destruction of the anterior horn cells of the rabbit by compression of the abdominal aorta, thus cutting off the supply of blood to the lower end of the cord. It is highly probable that anterior polio-myelitis is due to blocking of the anterior radicular arteries by inflammatory thrombosis, possibly of infective origin (Fig. 210), by which one or all the groups of cells in the anterior horn are destroyed, according to the extent of occlusion; thus patches of softening arise in the anterior cornua on one or both sides.

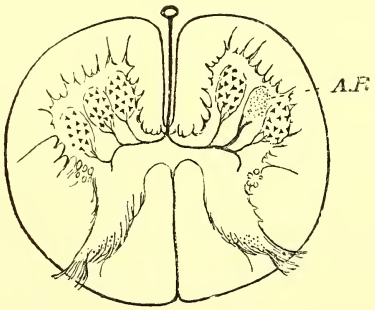


FIG. 210.—*Diagrammatic Representation of the Supply of the Groups of Anterior Horn Cells by the Radicular Branches of the Anterior Median Arteries.* Showing one group of cells completely destroyed by occlusion of one of these small vessels, and thus explaining why in polio-myelitis there is usually permanent loss of movement in some one or more muscles. (F. W. Mott.)

The appearances presented by the spinal cord may vary very considerably, according to the length of time which has elapsed since the onset of the disease. In an old case, examination of the segments of the spinal cord corresponding to the muscular paralysis (lumbar and cervical enlargements usually), exhibits a more marked translucency of the grey matter of the anterior horns; and if limited to one side, as it often is, a diminution in size of the anterior horn as compared with the opposite healthy side. The anterior horn cells are either absent, or here and there obtuse; or rounded protoplasmic bodies without processes, and staining well with carmine, are seen—probably vestiges of degenerated ganglion cells (Fig. 218). The fine nerve plexus around the cells is either greatly diminished or completely absent, and only neuroglia and Deiter's cells may be visible. The vessels are thickened. When the lesion is bilateral it is rarely symmetrical; more frequently it is unilateral, and it will then be observed that there is secondary atrophy of correlated structures of the same half of the cord—viz., of the posterior column, antero-lateral column and posterior horn, and some observers have described atrophy of the corresponding motor convolutions of the brain. Atrophy of anterior root fibres must occur. Atrophy of the bones has also been found.

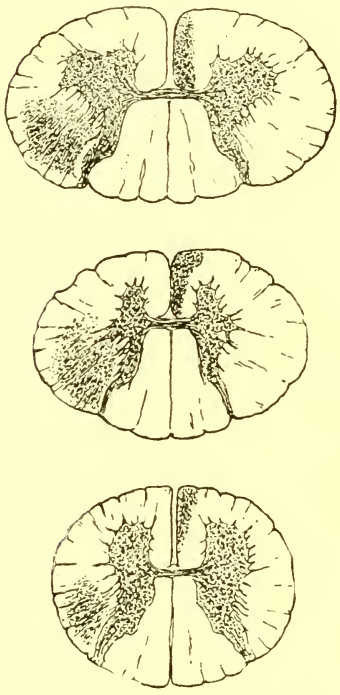


FIG. 211.—*Descending Degeneration in the Pyramidal Tract following Hæmorrhage into the Internal Capsule.* The direct tract is well marked and is represented at a lower level than it is usually seen. (F. W. Mott.)

Landry's paralysis (acute ascending paralysis): no definite lesion has been described; it may be due to the effects of a toxin acting upon the central or peripheral nervous system. *The absence of troubles of nutrition and sensibility* point to the poison acting, like curare, especially upon the motor tract, and serve to distinguish the disease from acute myelitis (p. 551).

Cerebral Hæmorrhage.

The various forms of softening which follow vascular occlusion have already been described. Cerebral hæmorrhage is the most frequent cause of hemiplegia in subjects who have passed forty; and, according to Gowers, it seldom occurs under that age, unless Bright's disease or aneurysm exists; the latter produced by infective embolism,

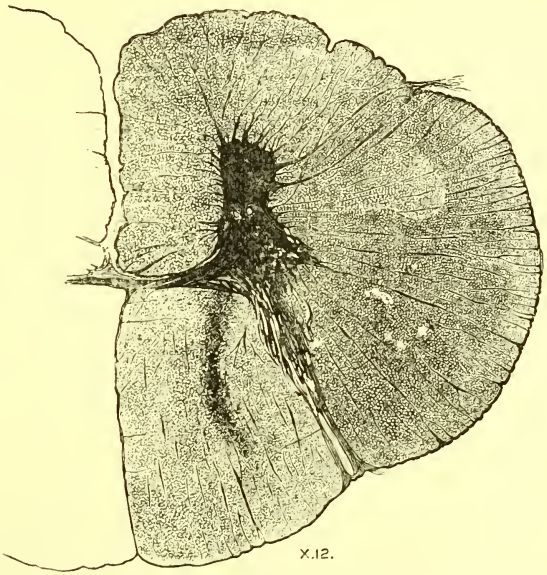


FIG. 212.—*Descending Degeneration in the Comma-shaped Tract and in the Intermedio-Lateral and the Crossed Pyramidal Tracts.* The drawing is made from a section of the spinal cord in the upper dorsal region just below the seat of compression of a small gumma. The direct tracts were in this instance small, not reaching into the dorsal region. The darkness of the comma tract is exaggerated, and the other descending degeneration is insufficiently represented. (F. W. Mott.)

and subsequent infective inflammation of the walls of the artery, which may eventually lead to its rupture. The association of granular, contracted or gouty kidney with apoplexy has long been recognised, the conditions being favourable to the rupture of the delicate cerebral vessels. It has been shown by Charcot that in most of these cases of hæmorrhage minute *miliary* aneurysms are found on the small vessels

entering the substance of the brain (p. 161); but there is one artery in particular, the left lenticulo-striate artery, which is especially liable to disease and rupture, and which has therefore been called "the artery of hæmorrhage." In Bright's disease there is high arterial tension, due to hypertrophy of the left ventricle and increased peripheral resistance. The small arteries which supply the basal ganglia come off directly at right angles from the large arteries at the base of the brain —they are terminal arteries, and, like all the intra-cerebral vessels, they are not supported by the substance of the brain, being surrounded by a perivascular lymphatic sheath. It is easy to understand, therefore, why aneurysms should form and rupture on these delicate walled vessels. Moreover, most authorities state that the vessel-walls are diseased. Charcot held that it was a periarteritis, while others affirm that it is an endarteritis.

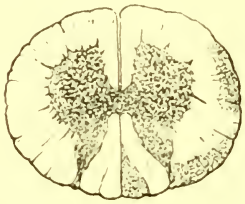


FIG. 213.—*The Ascending Tracts of Degeneration in the Cervical Enlargement after Experimental Hemisection of the Spinal Cord in the Mid-dorsal Region.* The section shows well-marked degeneration of Goll's column, of the direct cerebellar tract and of the antero-lateral tracts on the same side as the lesion. (F. W. Mott.)

Other conditions which predispose to cerebral hæmorrhage are lead, alcohol, syphilis, and inherited tendency to arterial disease. It may occur also in tumours.

The *effects produced* by hæmorrhage depend upon its situation and size; the most frequent seat is the anterior part of the opto-striate mass in the external capsule; but when paralysis occurs, as it usually does, the cause is damage of the pyramidal fibres of the hinder limb of the internal capsule. If the lesion be not severe enough to cause death, various changes occur in the effused blood and damaged nerve-tissues. For the first few days, the clot fills the whole cavity, and does not undergo shrinking; then a granulo-fatty degeneration takes place, with absorption of the products (p. 89).

In severe cases of hæmorrhage causing death, irruption of blood may take place into the lateral ventricle of the same side; then it may pass through the foramen of Munro into the opposite lateral ventricle. Occasionally, it may find its way from the third ventricle through the aqueduct of Sylvius and into the fourth ventricle; and, in rare cases, thence through the foramen of Magendie into the sub-arachnoid space.

Secondary Degenerations.

As a result of destruction of brain substance, secondary degenerations arise, the most characteristic of which is the secondary degeneration arising from destruction of the pyramidal cells of the motor area, or of their fibres in the anterior two-thirds of the posterior half of the internal capsule, such as occurs in cerebral hæmorrhage. It is quite obvious, however, that a similar degeneration may arise as a result of softening in embolism or thrombosis of the middle cerebral artery or its branches; in meningeal hæmorrhage and tumours, or, in fact, in any lesion which causes destruction of the pyramidal cells of the cortex of the central convolutions, or which cuts off the connection of the nerve fibres from the cells of which they are the outgrowths (Fig. 211).

As a rule, *cerebral lesions* leading to secondary degenerations are *unilateral*, and *spinal* are *bilateral*. In the former, only one set of pyramidal fibres are degenerated in the spinal cord—viz., those proceeding from one hemisphere by the internal capsule, the middle portion of the crus cerebri, the pons and the medulla, where the greater number decussate in the anterior pyramid to form the crossed pyramidal tract of the opposite side; some (about one-tenth) pass in the direct tract down the cord, decussating at lower levels.

Secondary degenerations arising from lesions of the spinal cord are, in nearly all cases, *bilateral*, and affect not only the *descending* tracts, which

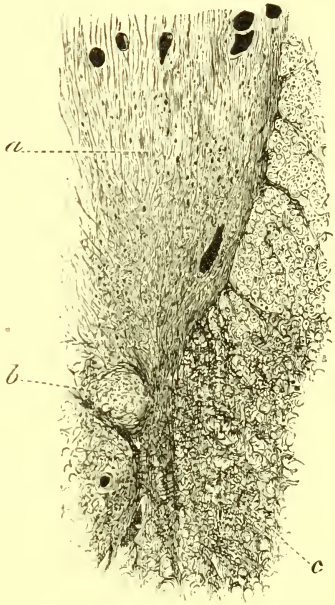


FIG. 214. — *Section of Spinal Cord about the eighth Dorsal Segment from a Case of Locomotor Ataxy.* There is sclerosis of the postero-external column and atrophy of the fine plexus of nerve fibrils surrounding the cells of Clarke's column; moreover, a band of sclerosis is seen entering the column instead of the bundle of nerve fibres. The cells themselves are atrophied and their processes destroyed. This case was of interest because, in connection with these lesions, the patient had well-marked visceral symptoms—gastric crises, bladder troubles, and laryngeal crisis—in addition to the ordinary ataxic symptoms. × 100 diameters. (F. W. Mott.)

have their centres of nutrition in the cortex cerebri, but also the *ascending* tracts, which have their centres of nutrition in the posterior spinal ganglia and grey matter of the cord. The ascending and descending *ground fibres*, which unite the different segments of the crus, pons, medulla, and cord together in co-ordinate reflex action, degenerate both above and below the lesion for a variable distance; and, besides, there is a small tract in the posterior column, which degenerates downwards in transverse lesions of the cord in the dorsal region; it is

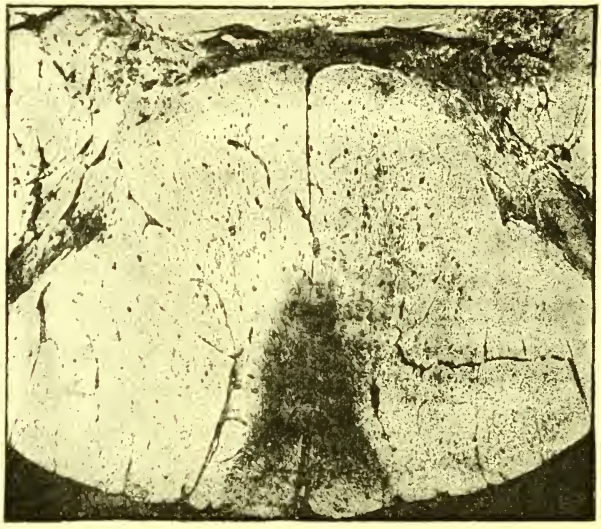


FIG. 215.—*Sclerosis of the Posterior Median Columns in the Cervical Region.* Due to spinal meningitis involving the posterior nerve-roots, fibres from which ascend, uninterrupted by cells, in the posterior median columns. (Specimen and photograph by F. W. Mott.)

termed, on account of its characteristic form, the *comma-shaped tract* (Fig. 212).

The ascending degenerations come under two classes.

(1) *In the Posterior Columns.*—Short, medium, and long coursing fibres, having their origin in the central portion of the T-shaped process of the posterior spinal ganglion cells.

The short fibres form Lissauer's tract, at the base of the posterior horn; the medium fibres enter the postero-external column, and, after a short course, disappear in the grey matter; and the long fibres, after entering the posterior column, are pushed backwards and towards the

median line to form the posterior median (Goll's) column. Secondary degeneration limited to the posterior column indicates a root lesion, such as from tumour of the cauda equina, or injury of posterior spinal roots (Fig. 215).

(2) *In the Antero-lateral Column.*—There are three sets of fibres occupying the periphery. They all arise from cells in the grey matter. The *posterior* tract consists of large fibres probably derived from axis cylinder projections of the cells of Clarke's column, and termed *direct, or dorsal cerebellar* tract. The *anterior,* consisting of two sets of fibres, in all probability arising from cells of the grey matter of the opposite horns, the decussation taking place in the anterior commissure. It has several names—viz., Gowers' tract, antero-lateral tract, and *ventral cerebellar* tract, because most of the fibres can be traced by a curious course to the middle lobe of the cerebellum. The less numerous fibres enter into the fillet, and probably end at the corpora quadrigemina.

The functions of these tracts—that is to say, the kind of impulses they conduct—is not known. At one time it was thought that all sensory impulses, except those of the muscular sense, decussated immediately on reaching the cord, and this view was held because in most cases of hemilesion of the spinal cord a group of symptoms occurs termed *Brown-Séquard paralysis,* which briefly is *hyperæsthesia and paralysis on the side of the lesion, and anæsthesia on the side opposite to it.* Latterly Brown-Séquard gave up the theory of immediate decussation of sensory impulses, but maintained justly that as a means of diagnosis the Brown-Séquard phenomenon was most valuable. Hemisection of the spinal cord in monkeys and other animals is followed by paralysis on the side of the lesion, but most recent observers have been unable to find either hyperæsthesia of the same side or anæsthesia of the opposite side (Fig. 213). For further information upon the conduction of sensory impulses, see p. 567.

The common causes of ascending and descending secondary degenerations of the spinal cord are focal lesions produced by injury, pachymeningitis in Pott's disease, meningitis, and tumours, causing a local transverse myelitis (p. 552).

Primary Pathological Degenerations.

Primary systemic degenerations may affect either the *afferent* sensory paths or the *efferent* motor paths, and not infrequently the two are combined.

1. **DEGENERATIONS OF AFFERENT TRACTS.**—These systemic degenerations have been looked upon as primary *scleroses*, the atrophy of the nerve fibres being secondary to overgrowth of the neuroglia connective-tissue and changes in the vessels. It is, however, more probable that the *sclerosis* is secondary to a progressive atrophy of the nerve fibres, brought about by retrogressive changes in the nutrition of the ganglion cells of which the nerve fibres are projections.

The causes of the nutritional degradation of the nerve cells are *inherited defect* and various functional excesses, by which they are unable, under altered conditions of the medium of nutrition, to maintain the nourishment of their axis cylinder processes—hence their degeneration.

The nutrient medium and its supply are especially liable to be affected by the poison of *syphilis, alcohol,* and *lead,* but inasmuch as each and all of these may also produce changes in the vessel walls, it is difficult to decide whether in many cases the vascular changes may not be primary to, or at any rate simultaneous with, the nutritional changes of the nerve cells and their processes.

Locomotor Ataxy or Tabes Dorsalis, is the commonest example of primary systemic degeneration of the afferent tract. Recent observations have shown that the peripheral nerves, as well as the posterior columns of the cord, undergo degeneration, and this supports the view of Marie that the primary change is a nutritional defect of the ganglion cells on the posterior root. In this disease there is not loss of motor power, but incoördination; and the motor efferent fibres of the peripheral nerves are intact, which tends to prove that the sensory fibres are selected; but in ordinary peripheral neuritis from alcohol both motor and sensory fibres suffer. A primary vascular change in the nerve fibres would affect both motor and sensory paths; again, it is difficult to understand how a primary vascular change in the cord should be confined to such

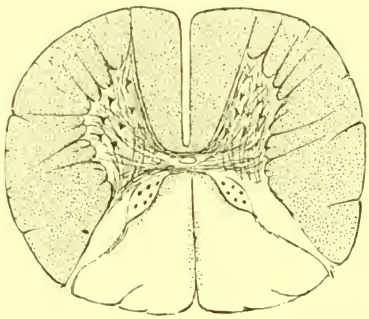


FIG. 216.—*Diagram to Represent the Lesion in an Advanced Case of Locomotor Ataxy.* The light parts indicate the sclerosis. It will be observed that nearly the whole posterior column is affected, and there is an atrophy of the fibres of the root-zone and of the plexus around the cells of Clarke's column, which appears clear, in consequence of the absence of the nervous reticule which exists in healthy spinal cords. The number of cells has not diminished. (F. W. Mott.)

narrow limits as the posterior column. If reference be made to Fig. 205, it will be seen that nutrient changes in the ganglion cells could produce simultaneous degeneration of the termination of their T-shaped processes. It has been ascertained that the ganglion cells of the posterior spinal ganglia are not destroyed in tabes, but their axis cylinder prolongations in the cord undergo degeneration and atrophy; consequently a *sclerosis* occurs in the three ascending tracts of the spinal cord previously mentioned—viz., Lissauer's tract, the postero-external column and root zone, and Goll's column. There will also be atrophy of the fine nerve network formed by the terminals of the postero-external column around the cells of Clarke's column (Fig. 214). In advanced ataxy, almost the whole posterior column may undergo atrophy or sclerosis (Fig. 216).

Morbid Anatomy.—To the naked eye the posterior columns have a grey transparent appearance on transverse section. The pia mater is usually thickened and adherent to the diseased parts. On microscopical examination two stages of degeneration may be recognised, corresponding more or less to the *preataxic* and *ataxic* periods.

The first is characterised by increase in the neuroglia tissue and slight swelling of the diseased parts; the second by *sclerotic atrophy.* It is especially the lumbo-sacral regions of the spinal cord which are affected. The earliest portions of the posterior columns to undergo degeneration are (1) the part external to Burdach's column lying in contact with the posterior horn (the root zone); (2) Goll's column; (3) Lissauer's tract. In an advanced case the remainder of the posterior columns and the network around the cells of Clarke's column are affected.

Histologically the process consists of wasting of the nerve-fibres in the tracts mentioned and overgrowth of neuroglia tissue; as the disease progresses the nerve-fibres waste and disappear, and the overgrowth of connective-tissue which proceeds from the vessel-walls and the trabeculæ coming in from the periphery, gradually replaces the nerve-fibres, and, by shrinking, produces *sclerotic* atrophy of the posterior columns. There is simultaneously a wasting of the peripheral nerve-fibres.

The first or preataxic stage is characterised by *absence of the knee-jerk, lightning pains, Argyll-Robertson pupils,* frequently *visceral crises, grey atrophy of the optic nerves,* and ocular paralyses.

The ataxic stage: *motor incoördination,* various sensory disturbances—notably numbness in the soles of the feet, and *inability to stand with the eyes shut—trophic disturbances* such as perforating ulcer, joint affections, and atrophy of bones, &c.

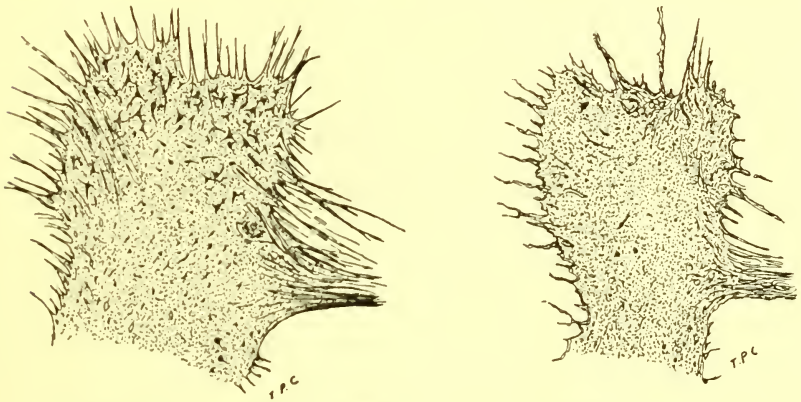
The visceral crises have been associated with affection of Clarke's column, but it is highly probable that they may be due to nutritional disturbances in the *sympathetic ganglia,* just as the other symptoms are supposed to be due to nutritional disturbances of the spinal ganglia of the posterior root. The loss of the knee-jerks is the earliest and most constant symptom; since the root-zone (bandelette of Charcot) is the earliest and most constant lesion of ataxy, it is highly probable that the loss of the knee-jerk is connected with the atrophy of those fibres derived from the third and fourth posterior lumbar roots, which on entering the spinal cord take up this position for a *short* distance before entering the grey matter (Fig. 206). Changes have been found in certain cerebral convolutions. It is possible that *tabes dorsalis* is a degenerative disease of the whole afferent tract.

Ataxic Paraplegia is a disease in which there is a combination of symptoms of lateral sclerosis and ataxy. The knee-jerks are exaggerated. The combined sclerosis of the lateral and posterior columns explains this condition.

Friedreich's Disease, or Hereditary Ataxy, is a lesion of the posterior columns, as in ataxy, but also an atrophy of the cells of Clarke's column, and consequently degeneration of the direct cerebellar tract; moreover, in some cases the crossed pyramidal tracts are affected. Beyond the hereditary history nothing is known of its ætiology. It may therefore be considered due to an inherited *developmental* defect, by which certain nervous structures undergo atrophy, and the neuroglia, hyperplasia.

2 **DEGENERATIONS OF EFFERENT TRACTS.**—The most important are—(1) primary lateral sclerosis; (2) amyotrophic lateral sclerosis; (3) progressive muscular atrophy. In all these diseases systemic degeneration of tracts of nerve fibres, vascular changes, and overgrowth of connective-tissue occur. Which is the primary process, the atrophy of the nervous elements or the vascular changes and *sclerosis?* The protoplasmic processes of the ganglion cells project into a lymph space which is in connection with lymph capillaries or with the perivascular lymphatics of the small vessels. It is common to find in chronic degenerative processes of the central nervous system periarteritis and distension of the perivascular lymphatics with leucocytes. It might be reasonably argued, therefore, that the poisons, such as alcohol, lead, and of syphilis (the most potent factor in the production of nervous disease), pro-

duced their effects by direct action upon the vessels. There are, however, instances of degeneration by no means uncommon—*e.g.*, amyotrophic lateral sclerosis and progressive muscular atrophy, in which none of these factors may exist; and the changes in the vessels and neuroglia must be considered, therefore, due to a primary atrophy of the ganglion cells and their processes. Strychnine and the toxins produced by the bacillus of tetanus and diphtheria, are examples of poisons which act directly upon the nerve cells or their processes; and Langley has shown that nicotine has a specially poisonous effect upon the cells of the peripheral ganglia. It is possible that syphilitic



FIGS. 217 & 218.—*Anterior Cornua from a Case of Polio-myelitis*, showing atrophy of the ganglion cells. For comparison the appearance of a healthy anterior cornua is shown. The small black triangles represent the cells as they appear under a low magnification. (F. W. Mott.)

toxins may vary in different individuals, or that hereditary defects may determine the seat of action of the toxic agency. In some people the vessels suffer first, in others the nerve cells, while in others again both vessels and nerve elements may be affected simultaneously.

Primary Lateral Sclerosis—termed "idiopathic," when there is no local disease affecting the path of the pyramidal fibres from the cortex. It is in all probability due either to a process of softening from vascular occlusion, or retrogressive nutritional changes in the cells of the cortex of the motor area by which the *pyramidal tracts degenerate.*

Progressive Muscular Atrophy and **Amyotrophic Lateral Sclerosis** are probably one and the same disease. In the former, the more common, the degeneration commences in the lower segment of

the motor path, and the primary change is in the anterior horn-cells (Figs. 217 and 218); but sooner or later the upper pyramidal segment of the motor path is affected. The changes in the anterior cornua and muscles resemble those met with in old anterior poliomyelitis already described. Clinically the affection of the pyramidal tracts is not demonstrable owing to the primary wasting of the anterior horn-cells and their corresponding muscles. In the amyotrophic form the process commences in the upper pyramidal segment of the motor path. There are, therefore, exaggerated deep reflexes, accom-



FIG. 219.—*Photo-micrograph of a Section of the Cervical Spinal Cord from a Case of Amyotrophic Lateral Sclerosis.* Degeneration of the crossed pyramidal and direct tracts and the antero-lateral ground fibres. The direct cerebellar tracts, the antero-lateral ascending tracts and especially the *posterior columns* are unaffected. There was almost complete absence of cells and fine nerve fibre reticulum in the anterior horns; this is observable by the difference in colour as compared with the posterior horns. (F. W. Mott.)

panied or followed by a progressive and characteristic wasting of groups of muscles owing to degeneration of the anterior horn cells (*vide* Figs. 219, 220, 221).

These cases of amyotrophic lateral sclerosis strongly support the view that there may be a primary retrogressive nutritional change in the ganglion cells, followed by a progressive wasting of their *neurons*, commencing at the terminals, and gradually spreading up the pyramidal tracts; because in some cases the degeneration has been found to extend only as high as the medulla, in others to the pons or crus; while in others, again, the internal capsule and the cortex have been affected. *Bulbar paralysis* is the same disease as progressive muscular atrophy, and is due to a degeneration affecting the motor nuclei of the

medulla, particularly a group of cells known as the glosso-labial laryngeal nucleus. It often forms the final stage of progressive muscular atrophy.

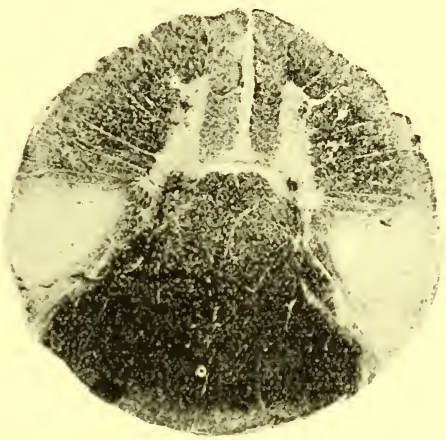


FIG. 220.—The same as previous figure, except that the section is of the seventh to eighth dorsal segments. The pyramidal tracts are *sclerosed*, and there is considerable degeneration in the intermedio-lateral tract. (F. W. Mott.)

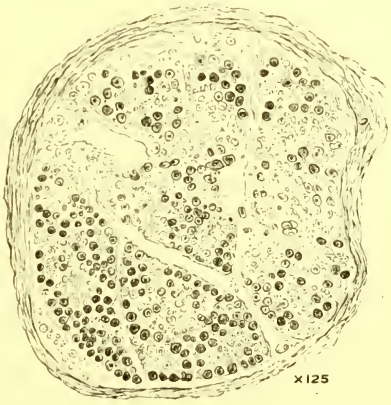


FIG. 221.—Drawing of a section of a fasciculus of the ulnar nerve from the same case, with atrophy of a great number of the fibres, stained with osmic acid. For account of the case from which these specimens were taken, *vide Brain*, vol. i. 1895. (F. W. Mott.)

General Paralysis of the Insane is considered by many authorities to be due to a primary nutritional change in the cells of the cortex cerebri. The ætiological factors of the disease are hereditary defect, alcohol, syphilis, mental overwork, sexual excess, and anxiety. The pathological process in the brain bears a resemblance to the changes in the cord in tabes. There is chronic thickening and opacity of the membranes, *peri-encephalitis,* the vessels are often gorged with blood, and their walls thickened and in a state of chronic inflammation. The perivascular lymphatic sheaths are distended and filled with leucocytes. The ganglion cells of the cortex are degenerated, some are swollen up, others atrophied, and there is an overgrowth of connective-tissue and increase of the glia-cells. Generally, the frontal lobes of the brain suffer first: the symptoms are varied and depend in a great measure upon the portions of the cortex which are most affected. Secondary degenerations of the spinal cord frequently occur. In some cases general paralysis may be associated with ataxy.



FIG. 222.—*Section of the Mid-dorsal Spinal Cord from a Case of Insular Sclerosis.* An islet of sclerosis, stained deeply, occupying no definite tract, is seen in the posterior column. (F. W. Mott.)

Insular Sclerosis. — Disseminated throughout the central nervous system in the grey and white matter, more often the latter, are varying sized *islets* of sclerosis, consisting of a feltwork of fine neuroglia fibrils (Figs. 222 and 223). This sclerosis, however, does *not* cause systemic Wallerian degeneration, because, although the myelin sheath disappears, the axis cylinders persist in the sclerosed tissue. The characteristic rhythmical tremors in intentional movement, may be due to the absence of the myelin sheath, by which voluntary impulses are not insulated in their passage along the pyramidal tract.

Syphilis may produce multiple disseminated patches of softening and sclerosis, but the axis cylinders are destroyed in the diseased foci, and, consequently, there is always secondary degeneration.

Syringomyelia.

This is a central gliosis of the spinal cord causing destruction of the grey matter and *excavation.* The usual seat is around the central canal in the *peri-ependymal* tissue, generally behind the canal, in the grey substance of the posterior commissure; thence it invades the

anterior and posterior horns. It is usually a neoplastic formation, but according to Charcot it may arise from a central myelitis. Its cause is unknown. The resulting symptoms are *muscular wasting,* and loss

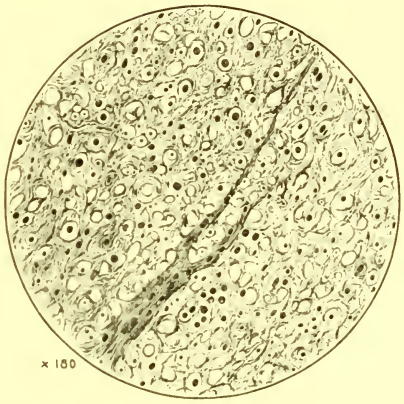


FIG. 223.—*Insular Sclerosis.* A small portion of the edge of an island of sclerosis seen in Fig. 222. Magnified 180 diameters. The section shows overgrowth of the neuroglia tissue at the expense of the white myelin sheath. The neuroglia stains deeply with carmine. Numbers of black dots are observable in the neuroglia; these are sections of naked axis cylinder processes, their myelin sheath having disappeared. There are some empty spaces in the section, but these are in all probability accidental. (F. W. Mott.)

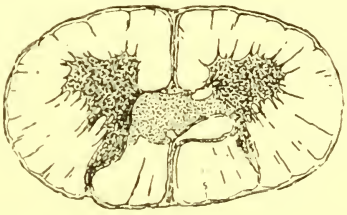


FIG. 224.—*Syringomyelia.* The section is from the cervical region and shows a central gliosis of the grey matter with excavation of the base of the right posterior horn. Lower down the excavation extended into the anterior horns on both sides. (F. W. Mott.)

of sensation to heat and cold, and painful impressions, but preservation of touch. This *sensory dissociation* is peculiarly characteristic of the disease, and goes to prove that Schiff was right in asserting that the

grey matter conducts painful sensations, and the posterior columns tactile and muscular sense impressions. The destruction of the anterior horns produces the muscular wasting, while that of the posterior horns the sensory disturbance, and, *possibly*, the trophic affections that often occur (Fig. 224). Of course the distribution of the motor, sensory and trophic changes will depend entirely upon the segments of the spinal cord affected. There may be unilateral destruction of anterior and posterior horns of the same side; and this has been found associated with motor paralysis and sensory disturbance of the same limb or side of the body.

Primary Progressive Myopathies.

The ætiology of this group of muscular atrophies is still obscure. Heredity plays a prominent part, especially through the maternal side. No definite pathological lesion of the central nervous system has been observed, and the disease is said to be a primary atrophy of the muscle fibres. *Pseudo-hypertrophic paralysis* (p. 96), and Erb's *juvenile paralysis*, are the best known types.

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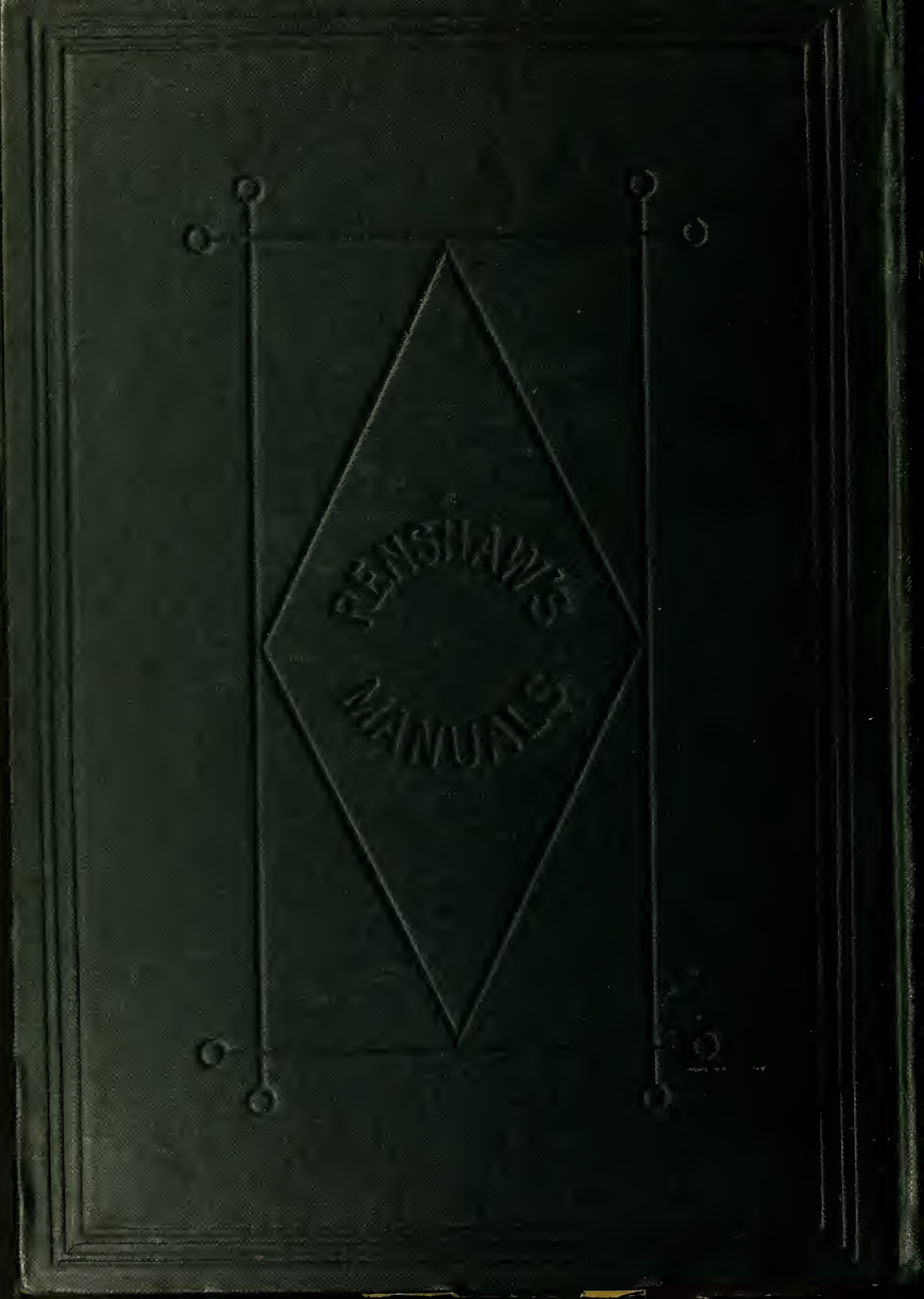
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